SECOND SERIES SEPTEMBER 1942 VOL. 18, NO. 9

BULLETIN OF THE NEW YORK ACADEMY OF MEDICINE

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Published monthly by THE NEW YORK ACADEMY OF MEDICINE
2 East 103 Street, New York

Entered as second-class matter, February 3, 1928, at the Post Office at New York, N. Y., under the Act of August 24, 1912. Subscription, United States, Canada and Cuba, $3.00; all other countries, $4.00 a year. Single copies, 50c.

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BULLETIN OF
THE NEW YORK ACADEMY
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SEPTEMBER, 1942

PHYSIOLOGIC STUDIES PERTAINING TO DEEP SEA DIVING AND AVIATION, ESPECIALLY IN RELATION TO THE FAT CONTENT AND COMPOSITION OF THE BODY

The Harvey Lecture, March 19, 1942

LIEUTENANT COMMANDER ALBERT R. BEHNKE, JR.
(MC), U. S. NAVY

THE environment again concerns the investigator. Beginning with the studies of Paul Bert, Heller, Mager, von Schrötter, and Haldane knowledge has accumulated slowly upon the effect of high pressures on the diver and caisson worker. The investigations conducted in the physiology laboratory of the Harvard School of Public Health in collaboration with the late Louis A. Shaw, and then at the Experimental Diving Unit, Navy Yard, Washington, D. C., have served to make possible rescue and salvage operations incident to a submarine disaster.

Recently these studies have clarified some of the puzzling phenomena observed in high altitude flight. In this lecture I shall outline the physiologic factors that enable divers and aviators to work in a pressure environment of 16 atmospheres or in a rarefied medium of 0.20 of an atmosphere, respectively. Of especial interest are the quantitative studies

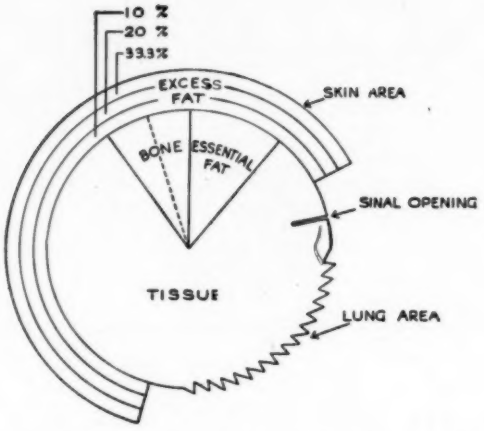

Fig. 1—Schematic representation of the body showing the volumetric relationship between the excess fat and the true body mass.

These data form the basis for the diagram—

Analysis of the true body mass, specific gravity=1.099

Substance	*Specific Gravity*	*Weight % Total mass*	*Volume % Total mass*
Bone	1.560	15	10.5
Essential Fat	0.940	10	11.7
Tissue	1.060	75	77.8

The addition of excess fat amounting to 10 per cent of total body weight reduces the specific gravity of the true body mass from 1.099 to 1.080; 20 per cent additional fat lowers the specific gravity to 1.062; and 33.3 per cent additional fat lowers the specific gravity to 1.036.

pertaining to the absorption or elimination of gaseous nitrogen which in turn have permitted estimates of fat content and composition of the body of the healthy, adult male.

With reference to the schematic diagram, Figure 1, protoplasm can be compressed or placed in a rarefied atmosphere without demonstrable effect provided that the pressure is equally distributed. Since air or other gaseous media are necessary for compression, interference with the free movement of gas, particularly in the channels leading to sinal and aural spaces, dilates blood vessels and produces hemorrhage into the occluded spaces. These painful but circumscribed effects of pressure are of minor importance, however, compared with the physiologic response brought about by the disturbance in gaseous equilibria whenever pressure fluctuates.

I. The Major Effects of High Barometric Pressure

1. *Nitrogen Narcosis.*—As the pressure is raised in an air atmosphere the ambient gases are absorbed by the circulating blood and transported to the other tissues of the body. Apart from the possible difficulty in opening the normally closed auditory tubes, it is perceived that as the air is warmed by the heat of compression, its increased weight calls forth greater respiratory effort which may interfere temporarily with the normal elimination of carbon dioxide. The outstanding phenomenon is that the previously normal individual loses his ability to function efficiently.[1,2]

Thus, the individual subjected to a pressure of 4 atmospheres, equivalent to a diving depth of 100 feet, begins to experience symptoms not unlike those elicited by altitude anoxia or alcoholic intoxication. Experienced divers, for example, are able to estimate diving depth within a range of 25 feet "by the way they feel." This feeling manifests itself as an impairment in neuromuscular coördination as well as a slowness and unreliability in cerebration. Essentially greater effort is required to perform work.

The agent responsible for the narcosis is "atmospheric nitrogen" including argon. When pure oxygen instead of air was breathed at a depth of 100 feet, the retardation, at least for short periods of time and prior to the onset of the symptoms of oxygen poisoning, was minimized. The employment of helium, moreover, to replace atmospheric nitrogen abolished or rendered negligible the adverse effect and proved that a rather ideal atmosphere could be created compatible with efficient work at depths up to 500 feet, and at a pressure not supporting consciousness were air breathed. By contrast, when argon was substituted for atmospheric nitrogen, the inhaled mixture at high pressures elicited reactions similar in type but more intense than those manifest in compressed air. Elementary gases, therefore, that are wholly innocuous at normal pressures may render an individual completely helpless in a high pressure atmosphere.

The explanation of the action of nitrogen and argon is to be sought in some physical property since argon does not possess valence and hence like helium, is incapable of entering into any stable chemical combination. Of the obvious physical properties solubility in oil and molecular weight may be important.

TABLE I

ARGON, HELIUM, NITROGEN, AND OXYGEN SOLUBILITY IN WATER AND IN OLIVE OIL AT 38° C., AND THE RESPECTIVE OIL WATER SOLUBILITY RATIOS

Water			
Argon	Helium	Nitrogen	Oxygen*
0.0262	0.0087	0.0127	0.023
Olive Oil			
Argon	Helium	Nitrogen	Oxygen
0.1395	0.0148	0.0667	0.112
Oil Water Solubility Ratios			
Argon	Nitrogen	Helium	Oxygen
5.32:1	5.24:1	1.7:1	4.9:1

* Sendroy, J., Jr., Dillon, R. T. and Van Slyke, D. D. *J. Biol. Chem.*, 1934, *105*:597.

The data in Table I are in accord with the Meyer-Overton hypothesis relating anesthetic effectiveness to fat solubility. The consideration that the higher molecular weights of nitrogen and argon might interfere with cellular gaseous metabolism particularly with carbon dioxide diffusion and transport has not yet been supported by experimental data.

The employment of hydrogen with a solubility coefficient in oil considerably higher than that of helium, may lead to the solution of the problem, or at least to an evaluation of the role that fat solubility in comparison with molecular weight assumes in the etiology of this type of narcosis.[3]

2. *Phenomena of Oxygen Poisoning.*—The increased partial pressure of oxygen in the air at great depths, the employment of oxygen as the basis for the decompression of divers and the treatment of compressed air illness, have necessitated extensive tests of oxygen tolerance.

At a pressure of 1 atmosphere pure oxygen has been inhaled by healthy men for periods as long as 17 hours without injurious effects. On the other hand, some individuals have complained of substernal distress and irritability following the inhalation of pure oxygen for periods of 7 hours. In one individual sensitivity to oxygen was manifest by the formation of wheals, dermatographia, flushing of the face, and later by

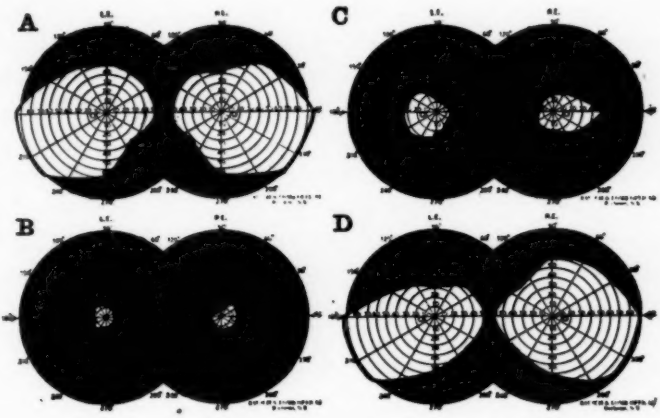

Fig. 2—Perimetric measurements made before and after 3½ hours' oxygen breathing at 3 atmospheres' pressure (30-lb. gauge). A, normal field limits; determinations made with the Ferree-Rand perimeter and exposure method with 7 foot-candles illumination. B, C, and D, field limits 5, 25, and 50 minutes, respectively, following 3½ hours' oxygen breathing; observations made at atmospheric pressure with a black perimeter of 25 cm. radius illuminated by a blue bulb placed behind and above the observer's head; moving stick stimuli were used and checked by the exposure method; test object was a white disc 6 mm. in diameter. From Behnke, Forbes, and Motley, *Am. J. Physiol.*, 1935-36, *114*:436.

the development of dermatitis. Remission of symptoms was hastened by the administration of histaminase. The action of a histamine-like substance, as postulated by Campbell,[4] explains many of the toxic symptoms associated with the inhalation of oxygen and suggests an approach to the solution of the problem.

At a pressure of 3 atmospheres the oxygen taken up by the blood in physical solution is sufficient to meet tissue requirements so that hemoglobin is not reduced.[5] Periodic waves of nausea constitute the most frequent symptom at this pressure together with the appearance of facial pallor. Progressive contraction of the visual fields terminating in a transient amblyopia has been repeatedly observed during the fourth hour of exposure.[6] Although vision is temporarily lost, a measure of consciousness is retained and recovery begins immediately upon the substitution of air for oxygen as illustrated by Figure 2.

Whenever doubt arises as to the habitability of a given environment, the decisive criterion is ability to work. An excellent test therefore of

resistance to the toxic effects of oxygen at a pressure of 3 atmospheres consists in having subjects exercise on a bicycle at a rate sufficient to increase oxygen consumption fourfold over the basal state. Test runs of this character are usually terminated after 15 to 20 minutes by extreme fatigue, numbness of the lower extremities, and in one instance by an abortive convulsive seizure. In control runs this type of exercise can be maintained without undue fatigue for a period of one hour.

In man, at a pressure of 4 atmospheres severe convulsive seizures occur after about 45 minutes of oxygen inhalation. Perhaps no other induced physiologic disturbance of comparable severity is followed by such prompt and complete functional recovery. Essentially oxygen induces transient idiopathic epilepsy in the apparently normal individual.

For periods of 27 minutes men have repeatedly inhaled oxygen at 4 atmospheres pressure with no other symptoms than a sensation of cerebral fulness and some degree of mental torpidity. Under these circumstances the excess quantity of oxygen taken up by the blood stream and held in solution in the tissues during a period of 17 minutes may augment oxygen absorption by 159 cc. per minute, a 55 per cent increase compared with the consumption during a control period. In the circulating blood of dogs exposed to 4 atmospheres pressure the oxygen in physical solution in arterial blood was 7 volumes per cent while the oxygen dissolved in the mixed venous blood was at times as high as 3.6 volumes per cent.

In the dog repeated daily seizures over a period of 21 days do not exert a detrimental effect on the well-being of the animal in that weight remains constant, appetite and muscular activity are unchanged. The tests indicate that tolerance for high oxygen pressure is developed because the exposure time necessary to produce the seizure is increased. Of particular interest are the recurrent strychnine-like seizures indicative of involvement of the spinal cord. During these attacks which are particularly apt to occur during the second diurnal exposure, the eyes turn outward, the whole body becomes rigid, the extremities spread apart, and opisthotonus supervenes. Tetanic contractions of the diaphragm stop respiration. These attacks may recur from four to twelve times per minute. The reflex excitability of the nervous system is greatly heightened since tactile, auditory, and visual stimuli serve to initiate the tetanic seizures.

Although these disturbances are severe, in view of the rapid recovery and the considerable latent period preceding onset of the symptoms, it has been possible to utilize oxygen in the prevention and treatment of compressed air illness.

3. *Field Application.*—The observations made in the laboratory soon governed field practice during diving operations in submarine disasters.

In 1939, divers breathing air at a depth of 240 feet in salvage work on the U.S.S. *Squalus,* suffered lapses of memory, mental confusion, and occasionally loss of consciousness. It proved to be not only dangerous but futile to work within a maze of hose and cables at a depth of 240 feet in an atmosphere of air.[7]

As in the laboratory, so also in the field, the substitution of helium for nitrogen rendered negligible the impairment in neuromuscular coördination and enabled divers to work efficiently when under 7 atmospheres of pressure. The successful termination of the salvage operations was made possible only by the employment of helium.

In 1940 a second submarine disaster occurred in water 440 feet deep. Although the pressure at this depth was sufficient to crush the hull of the disabled craft, divers breathing a mixture of helium and oxygen reached the bottom and were able to survey the sunken vessel. These divers, in spite of subjection to a pressure of 14 atmospheres, felt well and had little difficulty in performing the work required in descent and ascent to a depth corresponding closely to the height of the Washington monument.

II. Manner of Absorption or Elimination of Inert Gas

1. *Animal Experiments.*—The basic consideration concerned with existence in an abnormal pressure environment is the absorption and subsequent removal of inert gas. In this connection all of the gaseous nitrogen appears to be dissolved in fluids and fat in the ratio of 1 to 5 except for a small additional amount due to the presence of hemoglobin in solution. This molecular nitrogen can be removed from the tissues and measured if the body is placed in an oxygen atmosphere. Knowing the volume of the system and taking periodic samples it is not difficult to ascertain the quantity of nitrogen originally present in the tissues.

Dogs anesthetized by the injection of a suitable drug serve well for such experiments. If the first 7 minutes of an experiment be utilized to

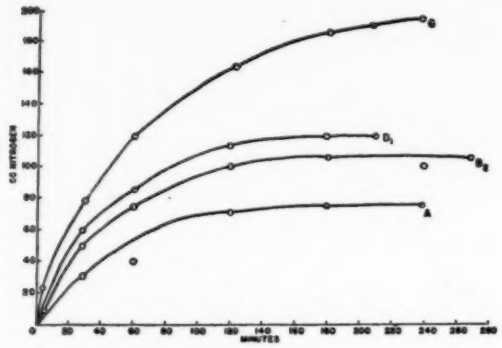

Fig. 3—Nitrogen elimination from 4 dogs placed in an oxygen atmosphere at normal pressure. During the first 7 minutes of oxygen inhalation the lungs and apparatus were rinsed free from nitrogen. (From Shaw, Behnke, Messer, Thomson, and Motley, *Am. J. Physiol.*, 1935, *112*:545.)

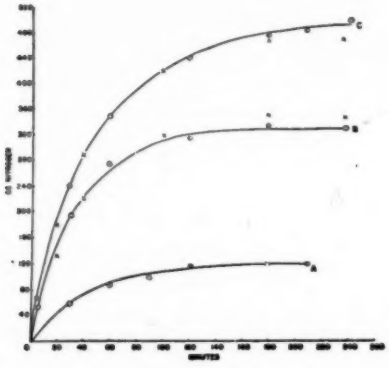

Fig. 4—The nitrogen elimination of dog "D" following equilibrium exposures in air at 1, 3, and 4 atmospheres of pressure. The nitrogen eliminated during the first 8 minutes of oxygen inhalation was not collected. Curve A, desaturation from 1 atmosphere; curve B, desaturation from 3 atmospheres; curve C, desaturation from 4 atmospheres. O, experimental values; ×, theoretical values. (From Shaw, Behnke, Messer, Thomson, and Motley, *Am. J. Physiol.*, 1935, *112*:545.)

rinse the lungs and apparatus free from nitrogen, then during a subsequent period of 3 to 4 hours the dog's body becomes nitrogen free.[8] Figure 3 represents a number of nitrogen elimination curves obtained on several dogs subjected to such a procedure at normal barometric

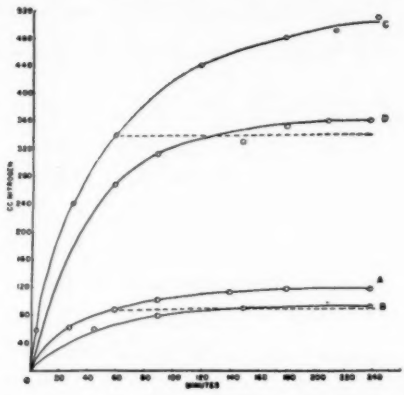

Fig. 5—Saturation time compared with desaturation time. Dog "D." The nitrogen eliminated during the first 7 minutes of oxygen inhalation was not collected. Curve A, follows complete saturation at 1 atmosphere; curve B, follows 67 minutes' saturation at 1 atmosphere; curve C, follows complete saturation at 4 atmospheres; curve D, follows 67 minutes' saturation at 4 atmospheres. (From Shaw, Behnke, Messer, Thomson, and Motley, *Am. J. Physiol.*, 1935, *112*:545.)

pressure. The fact that dog "G" was fat and dog "A" was lean is reflected by the large difference in the nitrogen content of the dogs in proportion to body weight.

If the dog is now placed in compressed air until saturation with ambient nitrogen has been attained, the nitrogen absorbed can be collected in the manner previously described. From a series of exposures in compressed air, utilizing the same dog "D," it was observed from the plotted data of Figure 4 that the amounts of nitrogen recovered following decompression from 3 and 4 atmospheres respectively, were proportional to the pressure. These results are in accord with Henry's law.

In another series of tests the rate of nitrogen absorption was compared with that of nitrogen elimination. Dog "D" was first rendered completely nitrogen free in the manner represented by curve A, Figure 5. For a period of 60 minutes the dog breathed air and following the air inhalation it was again placed in an atmosphere of oxygen. The amount of nitrogen absorbed during the 60-minute period of air inhalation, curve B, Figure 5, is equal to the quantity originally eliminated during the same period of time.

The same type of experiment was repeated at a pressure of 4 atmos-

pheres and again it was demonstrated that within the limits of experimental error, the manner of nitrogen transport is the same either to or from tissues.

Gaseous Nitrogen in Relation to Fluid and Fat Content of the Body.—If the body of dog "D" be subjected to analysis for the quantity of water, fat, and solid constituents, these values are obtained, body weight = 12.234 K., weight of fat* = 1.889 K., weight of dry solids = 3.117 K., weight of water (by difference) = 7.228 K. If these weights are multiplied by the appropriate solubility coefficients, the total nitrogen content of the body can be computed. Corrected for a pressure of 570 mm., for the density of fat, and for the decreased solubility of gas in body fluids when other dissolved substances such as salts are present, the coefficients adapted from Table I, are 52 cc.** per kilo of fat and 9 cc.† per kilo of fluid.

The nitrogen dissolved in the fat therefore is equal to 1.89×52, or 98 cc., and in fluids, 7.23×9, or 65 cc. The total nitrogen is 163 cc. or 1.3 cc. per kilo of body weight.

The quantity of nitrogen recovered from dog "D" was 124 cc. The difference between 163 and 124 cc. represents the estimated quantity of nitrogen given up during the first 7 minutes or rinsing period, and is in agreement with values based upon extrapolation of the experimental curve, that is 30 ± 5 per cent of the body total.

In practice, in order to avoid the use of extrapolated values, the quantity of nitrogen for the 7-minute period is taken as equal to the measured quantity obtained from the seventh to the twentieth minute as shown in columns 5 and 6, Table II.

The total nitrogen content of the body as measured by our technique, is distributed between fluid and lipid constituents of tissues.

Estimation of the Fat Content of the Body on the Basis of Measurements of Nitrogen Elimination.—In laboratory studies of gas absorption or elimination, it is of great importance to obtain an accurate estimate of the fat content of the body. From the discussion in the previous paragraph it is apparent this estimate can be made on the basis of meas-

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* Substances soluble in carbon tetrachloride.

** In the original paper a value of 55.7 cc. was used on the basis of analysis of omental dog fat. In all subsequent analyses we have used olive oil as a more convenient solvent since it has an absorbing capacity similar to that of body fat for nitrogen.

† In the original paper the value of 9.54 was used as the nitrogen solubility coefficient in water. It is more appropriate for body fluids, however, to use a coefficient approaching the solubility of nitrogen in serum. In urine analyses there is a decrease of 0.01 volume per cent of nitrogen for every two units increase in specific gravity. The value of 9 is closer to the true value than 9.54.

TABLE II

ESTIMATION OF THE FAT CONTENT OF THE DOG'S BODY ON THE BASIS OF THE MEASUREMENTS OF THE NITROGEN DISSOLVED IN THE TISSUES

Dog	*Weight* (1)	*Weight of fluids (60% body wt.)* (2)	*Nitrogen capacity of fluids* (3)	*Nitrogen capacity of fat* (4)	Total nitrogen capacity of body			*Weight of fat* (8)	*Weight of excess fat* (9)	*True body weight* (10)	*Fluid percentage of true body weight* (11)
					0-7′ (5)	7′-20′ (6)	Total (7)				
	kilos	*kilos*	*cc.*	*cc.*				*kilos*	*kilos*	*kilos*	
"D" lean	12.23	7.23	65	98	39	39	163	1.89	0.70	11.5	62
"A" very lean	8.8	5.28	48(+3)*	50(—3)	24	24	98	0.96	0.09	8.71	61
"B-2" lean	11.3	6.78	61	81	38	38	142	1.56	0.48	10.8	63
"D-1" lean	11.9	7.14	64	104	50	50	168	2.00	0.90	11.0	64
"G" fat	13.8	8.28	75(—5)*	183(+5)	65	65	258	3.52	2.38	11.4	71

* Optional correction to make fluid percentage of the true body weight a constant value of 63.

urement of nitrogen recovered from tissues and a knowledge of the water content of the body. The variability, however, in the amount of fat in different individuals renders invalid the employment of fixed percentages to denote the relative amounts of such body constituents as water.

This difficulty can be overcome by dividing the fat into an essential portion comprising such substances as myelin in the spinal cord, fat in bone marrow, lecithin, cholesterol and other lipid or lipoid matter essential in body economy, and a portion consisting of excess adipose tissue.

If one considers then that there is a basic body structure exclusive of excess fat as constant in composition as blood, which constitutes the true body weight, this weight can be divided into the following relatively fixed percentages: for the dog, water=63, solid substances=27, and essential lipids=10; for man, reflecting in part the difference in integument, water=66, solid substance=24, and essential lipids=10.

For the percentage of water in the body a tentative value of 60 may be used based on the analysis of dog "D."

The true body weights then of a series of dogs as well as the amounts of excess fat can be computed in the following manner using the data from dog "D" as an example:

Body weight$-12.23 \times 60 = 7.23$ weight of fluids.

$7.23 \times 9 = 65$ cc. nitrogen in the fluids.

$163 - 65 = 98$ cc. nitrogen dissolved in fat.

$98 \div 52 = 1.89$ kilos, weight of body fat.

$10/9\ (12.23 - 1.89) = 11.5$, true body weight.

$189 - 0.10\ (11.5) = 0.70$, excess fat.

$7.23 \div 11.5 \times 100 = 63$, percentage of water in true body weight.

The analytical data for the series of dogs are presented in Table II.

An initial value for water content of 60 per cent of the gross body weight may require some correction if the percentage of fluids in relation to true body weight is to be maintained at 63. With reference to dog "G," for example, a value of 60 per cent of total body weight for water content results in a final percentage of water of 71 in the true body weight, column 11 (Table II). Having determined the gross amount of body fat, it is not difficult to make the minor corrections in the division of nitrogen so that the water percentage in relation

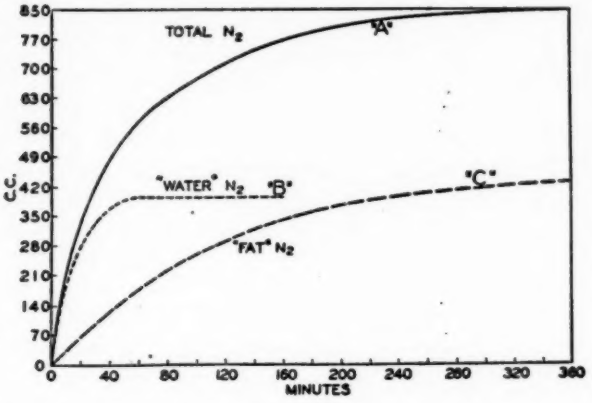

Fig. 6—Total N_2, A, represents the average of the values for nitrogen elimination from 3 men (average weight 64 k) who breathed pure oxygen at atmospheric pressure. "Water" N_2 (B) and "Fat" N_2 (C) are hypothetical curves showing the absorption or elimination of nitrogen by the body solvents. The values for nitrogen on A are approximately the sum of corresponding values on B and C. (From Behnke, *U. S. Nav. M. Bull.*, 1937, *35*:219.)

to true body weight is 63. The large difference between the solubility coefficients of nitrogen in water and in fat permit this correction without invalidating the estimate for fat. Of primary interest is the method of analysis rather than the attempt to maintain any given, fixed percentages in the calculations.

2. *Measurements in Man.*—If a human subject is placed in an enlarged oxygen recirculating system similar to that devised for the dog,[10] the gaseous nitrogen can also be removed from the tissues. Figure 6 shows the manner in which nitrogen is eliminated by lean men of comparatively small stature, average weight 64.2 kilos, if 99 per cent oxygen is inhaled for a period of 6 hours. It is observed that the rate of nitrogen output is about one-half of the corresponding rate for the dog, an anticipated finding in view of the comparative circulatory rates in relation to body weight.

If blood flow throughout the body were distributed uniformly with respect to the nitrogen content of tissues, the values of curve A could be derived from an exponential equation of the form $-Y=(1-e^{-kt})$ which expresses the relationship that a constant percentage of the nitro-

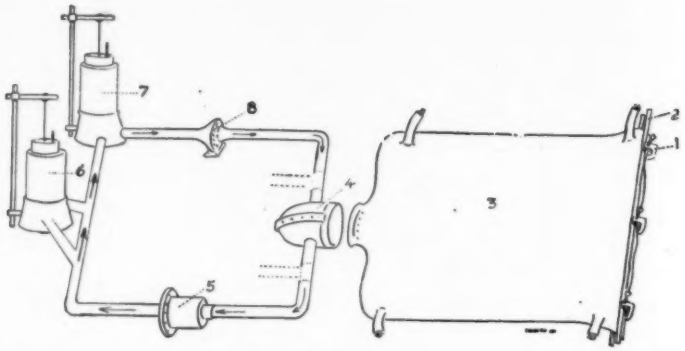

Fig. 7—Diagram of apparatus used to measure gas eliminated from the lungs and gas diffusing through the skin.

1, clamp on iron bars; 2, used to seal open end of rubber bag; 3, designed to fit around the body serving as a gas-tight seal; 4, rubber helmet and collar secured with adhesive tape around the subject's neck; 5, canister with absorbent for water and CO_2 cooled with ice; 6, spirometer for measuring added oxygen; 7, spirometer; 8, fan to circulate oxygen, bearing encased in oil to exclude air. Dotted lines indicate connections to a second similar system. (From Behnke and Willmon, *Am. J. Physiol.*, 1940-41, *131*:627.)

gen present in the body is being eliminated throughout the entire period of oxygen inhalation. In the equation Y = the amount of nitrogen eliminated during the time interval t; A = the initial nitrogen content of the body; k = the rate of change in the slope of the curve; and e is the base of the natural logarithms. The expression, $1-e^{-kt}$, gives the percentage decrease of nitrogen in the body during the time interval, t.

If the experimental values plotted on curve A, Figure 6, be substituted in the equation, the value for k is found to decrease progressively; a decrease that indicates that blood flow is not distributed uniformly in relation to the nitrogen content of tissues particularly in relation to fat which has a high nitrogen capacity and a poor blood supply. Thus, at the start of oxygen inhalation the average nitrogen pressure in the blood tends to fall below the nitrogen pressure in the fatty tissues which desaturate slowly. Consequently, the percentage rate of nitrogen elimination decreases.

However, if the total nitrogen content of the body is divided according to its solubility in water and in fat, then an equation can be applied similar to the one discussed in the previous paragraph but con-

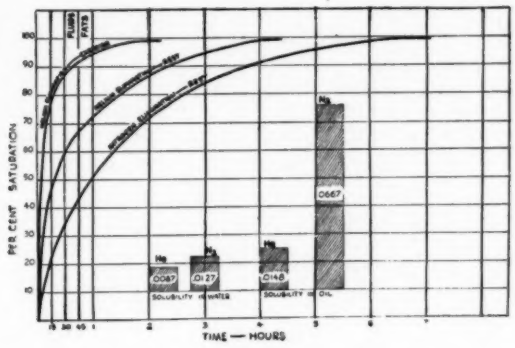

Fig. 8—Desaturation rate for man, comparing nitrogen with helium. During the first 45 minutes, gaseous removal takes place from the body fluids, and subsequently from the body fat. The solubility coefficients for helium and nitrogen are expressed as cubic centimeters of gas, reduced to standard conditions, dissolved per cubic centimeter of solvent, temperature 38° C.

sisting of two component parts, one for fat and the other for the body fluids. . . .

"Fluids" "Fat"

$$Y = 364\ (1-e^{-0.098\ t})\ \text{plus}\ 500\ (1-e^{-0.0085\ t})$$

The values for k will vary for different individuals on the basis of elimination rate and division of nitrogen between water and fat.

The previously described tests were terminated at the end of 6 hours so that the endpoint for nitrogen elimination was not known with certainty. Several years later, by means of the system outlined in Figure 7, it was possible to collect nitrogen from the tissues for periods as long as 17 hours. Table III gives the results of a test in which the subject, a diver weighing 70 kilos, breathed oxygen for a period of 15 hours. The data plotted in Figure 8 agree well with those obtained in the earlier tests if allowance is made for the difference in fat content of the subjects.

2. *Cutaneous Diffusion of Gases.*—Diffusion as a fundamental property of gases would lead one to expect some movement of gaseous molecules through skin.[11] This can be demonstrated by the arrangement, Figure 7, to permit the inhalation of oxygen in a hood while the body is surrounded by the same or an indifferent gas. In a representative ex-

TABLE III

NITROGEN ELIMINATION FOR A DEEP SEA DIVER, AGE 32, WEIGHT 154 POUNDS, HEIGHT 69 INCHES

Time	*Total eliminated*	*Nitrogen† diffusion into system*	*Net nitrogen*
min.	*cc.*		
0–5*	(150)		(150)
5–65	481	47	434
65–70‡	(25)		(25)
70–130	228	47	181
130–135‡	(12)		(12)
135–195	158	47	111
195–200‡	(7)		(7)
200–260	122	47	75
260–265‡	(5)		(5)
265–325	85	47	38
325–330‡	(2)		(2)
330–390	72	47	25
390–395‡			(–)
395–455	53	47	6
460–520	52	47	5
525–585	47	47	
			Total 1076
Body surrounded by oxygen			
595–655	46		
660–720	33		
725–785	34		
790–850	24		
Body surrounded by air			
855–905	48		

* Lung rinsing period. Estimated value of nitrogen elimination for this period.
† Diffusion of nitrogen into system includes atmospheric nitrogen diffusing through rubber tubing, helmet, spirometer water seal, and nitrogen diffusing through the skin.
‡ Represents a period of lung rinsing whenever a shift was made in spirometer systems. Nitrogen elimination values estimated for these periods.

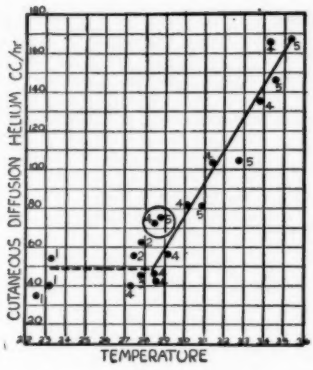

Fig. 9—Cutaneous diffusion of helium in relation to temperature, measured as cubic centimeters of helium recovered from the lungs per hour when the body is immersed in a helium atmosphere, pressure 700 mm. The numbers 1 to 5, refer to different subjects. The encircled values were obtained after the previously heated ambient helium had been cooled to 29° C. (From Behnke and Willmon, *Am. J. Physiol.*, 1940-41, *131*:627.)

periment following the prolonged inhalation of oxygen and when the body appeared to be nitrogen free, the substitution of oxygen for the ambient air in the bag brought about a sharp reduction in the quantity of nitrogen recovered from the lungs amounting to about 10 to 20 cc. per hour, Table III. This quantity of nitrogen, however, is only one-third to one-fifth the amount that one would expect to recover were diffusion sufficiently rapid to establish equality between the pressure of ambient nitrogen and its pressure in the skin and subcutaneous vessels.

The rapid diffusion of helium indicates the cutaneous penetration of gas. In experiments when helium was breathed, it was possible to recover from the lungs only about two-thirds of the helium, estimated on the basis of solubility in fluid and lipid constituents, to be present in the body following saturation in a helium atmosphere. Further, the demonstration that helium diffuses rapidly from the urine contained within the bladder walls of divers subjected to rapid decompression from high pressure, suggested that the outward diffusion of helium through the skin accounted for the one-third or greater discrepancy between the pulmonary measurements and the estimated helium content of the body.

If the subject breathes air or oxygen in a hood and the body is surrounded with helium, then a constant volume of helium will be excreted by the lungs after 30 to 60 minutes, provided that the temperature of the gas in contact with the skin is controlled.

In Figure 9, the relationship is apparent between the helium collected in the spirometer and the temperature of the ambient helium in the bag surrounding the subject's body. The abrupt linear rise in the amount of gas diffusing through the skin in the range of 28° C., and upward is explained chiefly on the basis of increased cutaneous blood flow. There is in fact a close correspondence between the computation of peripheral blood flow on the basis of heat loss from the body as demonstrated in the calorimeter, and on the basis of diffusion of helium through the skin. In contrast with nitrogen, the diffusion of helium is so much greater that equality appears to be established promptly between the pressure of the ambient helium and its pressure in the skin and underlying blood vessels.

3. *The Helium Elimination Curves.*—If the nitrogen that is carried away from the tissues after the first 40 to 60 minutes of oxygen inhalation has its depot in fatty tissue then helium possessing a low fat solubility coefficient should be eliminated faster and in smaller quantities during a corresponding period of time.[12] Following exposure in a helium-oxygen atmosphere it is observed that the absorbed gas leaves the body in about one-half of the time required for nitrogen removal and that the plotted data, Figure 8, resemble the nitrogen curves characteristic of the dog. The amount of helium both in percentage of the body total and the actual quantity eliminated after the first hour are small compared with nitrogen. During exercise sufficient to increase oxygen consumption threefold, almost all of the helium was eliminated during the first 15 minutes, and after 40 minutes 90 per cent of the helium had left the body.

4. *The Field Test of Decompression.*—There is yet a better way to demonstrate the difference in the capacity of fat to absorb nitrogen compared with helium. In diving operations and caisson work the length of time required for decompression is a good index of the quantity and rate of removal of gas absorbed in the tissues.

Although about 75 per cent of the total body nitrogen is given off at a comparatively rapid rate in depths up to 100 feet, and hence does not usually contribute to the development of "bends," there appears

TABLE IV

COMPARISON OF TOTAL DECOMPRESSION TIME FOLLOWING EXPOSURE IN COMPRESSED AIR AND EXPOSURE IN A HELIUM-OXYGEN ATMOSPHERE

Depth	*Exposure*	*Recompression**	
		Air	*Helium-oxygen*
ft.	*min.*		
90	100	50	75
90	180	...	77
90	360	...	79
90	540	638	79
150	80	141	121
150	180	...	126
150	360	...	128
200	65	217	154
200	90	...	164

* Time in minutes.

to be a relatively small amount of gas dissolved in the fat of bone marrow and in the spinal cord that requires many hours for removal. Following an exposure of 9 hours (probable saturation) in compressed air simulating a depth of 90 feet, a period of 10½ hours was required for decompression. On the other hand, a 2-hour exposure (75 per cent saturation) at the same depth required only 60 minutes for decompression. In tissues other than bone marrow and the spinal cord, gaseous diffusion and a greater circulation of blood tend to equalize nitrogen pressure throughout the body. Are the greater nitrogen uptake, the limitation of diffusion by bony walls, and the sluggish, sinusoidal circulation the factors responsible for the slow decompression necessary after long exposures in compressed air?

By contrast, the properties of helium render this gas ideal for diving and the decompression time following saturation in a compressed helium-oxygen atmosphere is not only greatly reduced but no appreciable decompression is required in excess of one hundred minutes' exposure as shown in Table IV. With reference to helium, the period of

decompression of 79 minutes stands in contrast with the corresponding period of 10½ hours required for air. Thus, the test data obtained from rapid decompressions corroborate the laboratory analysis as to the contrasting behavior of nitrogen and helium.

III. Physical Qualifications for Work in Abnormal Pressures

1. *The Altitude Tolerance Test.*—The selection of individuals resistant to "bends" and other ills incident upon decompression has been difficult. *A priori,* one might select men devoid of excess fat since every kilogram of adipose tissue absorbs 52 cc. of nitrogen per atmosphere of pressure. A second important consideration, in view of the manner of gas transport, would be circulatory efficiency in the sense of good cardiac output and adequacy of collateral circulation. Degree of cardiovascular tone and age therefore would appear to be important criteria. Yet susceptibility to "bends" could not be predicated on the basis of these qualifications alone. Essentially it was necessary to know for each individual his resistance to the ill-effects of decompression by means of a specific test.

To meet this practical need, individuals were exposed to an atmosphere equivalent to a depth of 100 feet for a period of 28 minutes. The subsequent rapid decrease in pressure to normal during a period of 2 minutes induced symptoms in susceptible individuals but the test had obvious disadvantages in that, not only was an undetermined quantity of nitrogen absorbed during the 28-minute period of exposure that fell far short of saturation, but symptoms elicited by the test required recompression treatment.

These disadvantages were overcome by an experiment in which the normal barometric pressure was decreased rapidly in what may be termed an altitude tolerance test.[13] The simulated altitudes to be reached range from 30,000 to 40,000 feet at a rate of ascent of 5,000 feet per minute, and the duration of stay at the designated altitude is one hour unless aeroembolism supervenes. Oxygen was breathed continuously in these tests.

The results of sixty tests indicated that twenty-eight divers and aviators were able to remain free from symptoms at or above an altitude of 34,000 feet. On the other hand, thirty-two divers and aviators developed "bends" and occasionally incipient asphyxia. The lowest altitude at which symptoms occurred was 27,000 feet. Areas of old injury

proved to be frequent sites for the location of the characteristic pain associated with "bends." This test has served to classify aviators as to their ability to remain free from symptoms at altitudes above 30,000 feet, and deep sea divers as to their resistance to compressed air illness. The divers, for example, who descended to depths of 440 feet in search of a disabled submarine, and ascended safely to the surface, were men who were able to remain free from symptoms for a period of one hour at a simulated altitude of 40,000 feet.

2. *The Specific Gravity of the Body as an Index of Obesity.*—Our problems as analyzed in this lecture are intimately concerned with the amount of fat in the body. Measurements of the nitrogen dissolved in the tissues yield data which may be used to estimate fat content but the procedure is too tedious for routine determinations.

A direct method that serves effectively is the measurement of the specific gravity of the body as a whole, essentially a determination of the density of corporeal tissue in relation to unit volume.[14,15] This objective is attained by weighing an individual in air and in water. The relationship between the loss of weight in water and the weight in air is an index of the density of the tissues. The influence of fat, possessing as it does the lowest density of any body constituent, is apparent.

It is not necessary to go into details as to procedures. It suffices to state that the proper method, taking due care to measure the residual air volume, has enabled us to classify men as to their degree of obesity on the basis of the outlined principles. Fat men tend to float in water and values in the range of 1.030 for specific gravity are characteristic of these individuals. On the other hand, for a group of lean men in the Naval Service, average weight 150 pounds, the mean specific gravity was 1.080. For a group of professional football players, although their weight was 200 pounds, the mean specific gravity was also 1.080 ± 0.001. This fact tends to show that it is the inherent composition of tissue rather than the absolute weight that governs specific gravity.

3. *The Composition of the Human Body.*—It has been helpful in the study of the effect of the abnormal pressure environment on the individual to consider the body as a mass of essential tissue separate from the excess fat. In the completion of our analysis various fragments of knowledge can be assembled into a mosaic that reveals the composition of the true body mass as relatively constant under controlled conditions for individuals of the same sex and age groups, realizing that eventually

TABLE V

COMPOSITION OF THE BODY

Substance	*Specific gravity*	*Water*	*Solid constituents*		*Basic body composition equivalent combinations sp. gr.* 1.099+0.001	
			Percentage	*Specific gravity*	*Substance*	*Percentage*
		Per Cent				
Blood	1.060	80	20	1.4		
Tissue	1.060	80	20	1.4	Tissue Bone Fat	75.0 15.0 10.0
Bone	1.56	30	70	1.68		
0.5 Calcium salts	3.00			3.0		
0.5 Tissue	1.060	80	20	1.4	Tissue Bone salts Fat	82.5 7.5 10.0
Fat	0.94				Water Solids Bone salts Fat	66.0 16.5 7.5 10.0
Body as a whole	1.099	66	16.5 7.5*	1.4 3.0	Water Solids Fat	66.0 24.0 10.0

* Calcium salts in bone.

quantitative analyses will define the range in variation of such constituents as bone and fluids.

The true weight of the body, therefore, as represented by Figure 1, is assumed to consist of 15 per cent bone, 10 per cent essential lipids, and 75 per cent tissue. The specific gravity of this mass then can be computed on the basis of the following data:

Bone is frequently analyzed as containing 50 per cent mineral substance, largely calcium salts to which a specific gravity value of 3 may be assigned. The other half of bone amounting to 7.5 per cent of the body weight may be classed as tissue.

The specific gravity of the lipids is of the order of body fat, 0.94, a value obtained experimentally on the basis of actual fat loss in relation to specific gravity.

For tissues a value for specific gravity of 1.060 is the same as that obtained by repeated determinations of whole blood withdrawn from the above mentioned test subjects. Analyses for individual tissues ac-

TABLE VI

EFFECT OF EXCESS FAT ON THE SPECIFIC GRAVITY OF THE BODY

Basic composition	*Weight units*	*Volume units*	*Specific gravity*	*Specific gravity determinations of 174 Naval personnel*		
				No. men	*Range of specific gravity*	*Difference thoracic, abdominal circumference*
Tissue	75.0	70.75				
Bone	15.0	9.62				
Essential lipids	10.0	10.70				
	100.0	91.07	1.099	21	1.090—1.099	7.2
10 per cent	100.0	91.07				
excess fat	11.1	11.82		30	1.080—1.089	6.3
	111.1	102.89	1.080	41	1.070–1.079	5.5
20 per cent	100.0	91.07				
excess fat	25.0	26.60		41	1.060–1.069	5.2
	125.0	117.67	1.062	31	1.050–1.059	4.3
				5	1.040–1.049	4.2
33.3 per cent	100.0	91.07		3	1.030–1.039	0.9
excess fat	50.0	53.76		2	1.020–1.029	–0.1
	150.0	144.83	1.036			

cording to Vierordt,[16] give values of the order of 1.014 for pericardium to 1.1219 for tendon; e.g., muscle, 1.051, brain, 1.040, liver, 1.057. For tissue it may be assumed that the distribution of water and solid constituents is in the ratio of 80 to 20. In accord with this distribution the specific gravity of the solid residuum is 1.40.

The analysis of the composition of the body is summarized in Table V, showing the values used for blood, tissue, bone, fat, and solid constituents. The basic composition of the body can be analyzed in several ways as long as the ratios of the constituent substances or their equivalents are not altered with respect to body weight. The same value for specific gravity of 1.099, representing the true body mass, is therefore applicable to any group arrangement of constituent substances, as shown in the table.

If to the true corporeal structure, excess adipose tissue be added in percentages of 10, 20 and 33.3 of the total body weight, the respective values for specific gravity will be 1.080, 1.062, and 1.036 corresponding

TABLE VII

BODY COMPOSITION AND SPECIFIC GRAVITY OF A DEEP SEA DIVER COMPUTED FROM THE GASEOUS NITROGEN CONTENT OF THE BODY
(See Table III, Page 576)

Body weight	= 70 kg.	Total nitrogen	= 1,076 cc.
Weight fluids	= 70 × 0.60		= 42 kg.
"Water" nitrogen	= 42 × 9		= 378 cc.
"Fat" nitrogen	= 1076 — 378		= 698 cc.
Weight fat	= 698 ÷ 52		= 13.4 kg.
True body weight	= 10/9 (70 — 13.4)		= 63 kg.
Excess fat	= 70 — 63		= 7 kg.
Ratio $\frac{\text{Weight water}}{\text{True body weight}}$			= 66 6
Corrections—			
Water, 0.66 × true body weight			= 41.58 kg.
"Water" nitrogen	= 4.58 × 9		= 374 cc.
"Fat" nitrogen	= 1076 — 374		= 702 cc.

Specific gravity of the body, computed—

True body weight	*Weight (units)*	*Volume (units)*
Water	41.58	41.58
Fat	6.30	6.77
Solid constituents	15.12	9.00
	63.00	57.35

SPECIFIC GRAVITY = 63 ÷ 57.35 = 1.098

True body weight plus excess fat = 63 + 7 ÷ 57.35 + 7.53 = 1.079

Specific gravity of the diver's body as determined by the method of water displacement = 1.060

to the division of Naval personnel into three groups on the basis of high, intermediate, and low specific gravity measurements.

On the basis of determinations of specific gravity the value of 1.099 is higher by two units than the top figure obtained in a series of 200 tests in which healthy individuals between the ages of 20 and 40 served as subjects. Men possessing the highest values therefore have no excess fat and their bodies contain only about 10 per cent by weight of lipid matter that is regarded as essential. A reading for specific gravity of 1.080, or approximately the average for the high group, is indicative of the presence of 10 per cent *excess* fat, a figure of 1.062 indicates the presence of 20 per cent *excess* fat, while a value of 1.036 obtained on several fat men denotes that 33.3 per cent of the body weight consists of *excess* fat, Table VI.

The analysis applicable to the diver whose nitrogen measurements extended over a period of 15 hours, Table VII, summarizes the results with reference to the estimation of the fat content of the body both on the basis of measurements of nitrogen elimination and determination of specific gravity. In this particular example some discrepancy exists between the specific gravity as measured, and the specific gravity as computed on the basis of excess fat in relation to basic body structure. But undoubtedly quantitative data obtained in the future as to the relative amounts of the constituents in the true body mass will diminish the difference.

REFERENCES

1. Behnke, A. R., Thomson, R. M. and Motley, E. P. The psychologic effects from breathing air at 4 atmospheres pressure, *Am. J. Physiol.*, 1935, *112:*554.
2. Behnke, A. R. and Yarbrough, O. D. Respiration resistance, oil-water solubility and mental effects of argon, compared with helium and nitrogen, *Am. J. Physiol.*, 1939, *126:*409.
3. Case, E. M. and Haldane, J. B. S. Human physiology under high pressure, *J. Hyg.*, 1941, *41:*225.
4. Campbell, J. A. Oxygen poisoning and tumor growth, *Brit. J. Exper. Path.*, 1937, *18:*191.
5. Behnke, A. R., Shaw, L. A., Shilling, C. W., Thomson, R. M. and Messer, A. C. Effect of high oxygen pressure upon the carbon-dioxide and oxygen content, the acidity, and the carbon-dioxide combining power of the blood, *Am. J. Physiol.*, 1934, *107:*13.
6. Behnke, A. R., Forbes, H. S. and Motley, E. P. Circulatory and visual effects of oxygen at 3 atmospheres pressure, *Am. J. Physiol.*, 1935-36, *114:*436.
7. Behnke, A. R. and Willmon, T. L. U.S.S. Squalus; medical aspects of rescue and salvage operations and use of oxygen in deep-sea diving, *U. S. Nav. M. Bull.*, 1939, *37:*629.
8. Shaw, L. A., Behnke, A. R., Messer, A. C., Thomson, R. M. and Motley, E. P. The equilibrium time of the gaseous nitrogen in the dog's body following changes of nitrogen tension in the lungs, *Am. J. Physiol.*, 1935, *112:*545.
9. Behnke, A. R., Thomson, R. M. and Shaw, L. A. The rate of elimination of dissolved nitrogen in man in relation to the fat and water content of the body, *Am. J. Physiol.*, 1935-36, *114:*137.
10. Behnke, A. R. Application of measurements of nitrogen elimination to the problem of decompressing divers, *U. S. Nav. M. Bull.*, 1937, *35:*219.
11. Behnke, A. R. and Willmon, T. L. Cutaneous diffusion of helium in relation to peripheral blood flow and the absorption of atmospheric nitrogen through the skin, *Am. J. Physiol.*, 1940-41, *131:*627.
12. Behnke, A. R. and Willmon, T. L. Gaseous nitrogen and helium elimination from the body during rest and exercise, *Am. J. Physiol.*, 1940-41, *131:*619.
13. Behnke, A. R., Jr. Investigations concerned with problems of high altitude flying and deep diving; application of certain findings pertaining to physical fitness to the general military service, *Mil. Surg.*, 1942, *90:*9.
14. Behnke, A. R., Jr., Feen, B. G. and Welham, W. C. An index of obesity, *J.A.M.A.*, 1942, *118:*495.
15. Welham, W. C. and Behnke, A. J., Jr. Physical characteristics of exceptional athletes and of naval personnel, *J.A.M.A.*, 1942, *118:*498.
16. Vierordt, H. *Anatomische, physiologische und physikalische Daten und Tabellen.* 3. ed. Jena, Fischer, 1906.

SURGICAL TREATMENT OF PERIPHERAL EMBOLISM AND ANEURYSM*

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FROM the first World War sufficient experience in the treatment of wounds and diseases of the vascular system was derived to form a basis for the treatment of lesions of this system. With our entrance into the second and greater World War the practical application of these principles will be put to the test in an immediate and wide field. In the treatment of peripheral embolism and aneurysm these principles must be used. An enumeration and discussion of them is even more timely than it was thought when the subjects were presented at the Graduate Fortnight. While many of the principles arising in the treatment of both of these conditions are similar, they will be discussed separately for clarity.

I. PERIPHERAL EMBOLISM

In arterial embolism there is a sudden and complete closure of a major vessel. Shock is inevitably present and, unless therapeutic efforts are successful, the loss of the limb and, in a high percentage of cases, the life of the individual results. The final closure of a vessel already chronically occluded is another picture, because in such chronic closures collateral circulation channels have already been prepared. Surgical treatment of peripheral embolism until recently—and unfortunately in some places still—has been confined to major amputation, if the patient survived until demarcation was complete. Fortunately, surgical therapy has been proven sufficiently successful so that a fair percentage can be saved, not only from death, but from the previous major amputation.

Peripheral embolism is accompanied by a left side heart disease in four out of five instances. Usually there is the added insult of auricular fibrillation, severe infection or an operative procedure. The paradoxical occurrence of an embolus from the right side of the heart or the peri-

* Delivered October 17, 1941, at the Graduate Fortnight of The New York Academy of Medicine.

TABLE I

SITE OF PERIPHERAL EMBOLI

Site	*Rate of Occurrence*
Aorta	4.5
Iliac	17.3
Femoral	54.5
Popliteal	11.3
Arm	12.1
Tibial	.5

pheral venous system requires a patent foramen ovale. In arterial disease a local trauma may loosen a plaque which becomes an embolus, but more often this results in thrombosis.

Symptoms: Pain is inevitably present and it is sharp and severe. *Tenderness* follows the embolus and is greatest at the site of its lodgement. The *color* of the limb changes to a white, dead-like appearance, followed by a blotchy discoloration and eventually gangrene. The *reflexes* are absent and there is a paralysis of the part. With the *color change*, the part becomes *cold*. Oscillometric readings and blood pressure are zero.

Differential Diagnosis: If there is a diseased heart, which is fibrillating and has an added strain with the symptoms already enumerated, a diagnosis of embolus is indicated. *Arterial thrombosis* must be differentiated. In arterial thrombosis there is evidence of failing arterial circulation for some time and arteriosclerotic changes in other vessels, either by palpation or x-ray examination. Occasionally the differential points are not clear until operation time. *Acute thrombophlebitis* should not be difficult to differentiate, as in this condition the foot is warm, enlarged and cyanotic with distended veins. There is normal arterial circulation as shown by palpation and oscillometric readings.

Pathology: At the site where the embolus lodges in the intima an inflammatory process develops. There is swelling of the walls of the vessels and later destruction of the intima. The embolus usually lodges at the bifurcation of an artery, where the lumen of the vessel rapidly becomes smaller. The most common site is at the bifurcation of the femoral and femoral profunda arteries, the internal and external iliac, the bifurcation of the abdominal aorta and the division of the anterior posterior tibial arteries (Table I).

Spasm of the involved vessel and the collateral vessel is invariable and may be a factor in the pain (Lund, McKettrick and Allen). This spasm has a physiological basis, as it prevents the formation of a thrombus below the embolus site. If this spasm is relaxed before adequate therapeutic measures have been instituted, the entire vessel below the embolus may be entirely closed. Occasionally the spasm of the collateral circulation will relax sufficiently to permit a degree of circulation to be established around the embolus. Thrombosis occurs in 50 per cent of patients with an embolus. This is one of the reasons for doing early embolectomy, as other conservative measures are unable to restore circulation when the thrombosis is present. There is a definite difference between the closure of a major artery by an embolus and by a ligation. Halstead in 1924 was unable to find gangrene occurring from ligation of the subclavian artery and Mulvihill reported an incidence of only 14.7 per cent gangrene in sixty-seven ligations of the common iliac, external iliac and femoral arteries. Wolf found that 50 per cent of the ligations of the common iliac artery resulted in gangrene, while only 15 per cent of the ligations of the popliteal arteries affected the circulation. In the arm a mere 5 per cent of the brachial artery ligations were followed by gangrene. In a ligation of an artery the collateral circulation is frequently adequate. After embolus, however, the thrombus which frequently forms, extends into collateral branches and prevents their function, even if spasm can be relieved.

Treatment: The names of the surgeons who first tried embolectomy are those whose surgical work has been outstanding. Abanejew performed the first exploration for peripheral embolus in 1895, but failed to locate one. Moynihan, in 1897, removed an embolus from the popliteal artery, but the patient died. In 1907 both Stewart and Doberauer removed emboli with temporary benefit, but thrombosis followed shortly thereafter. Trendelenburg's first effort on pulmonary embolism was in 1907, the patient dying of hemorrhage on the table. In 1908-09 Proust, Schussi, Murphy, Carrel and Leriche all tried the operation with failure. The first successful embolectomy (Lahey, in 1911) was followed shortly thereafter by Key in Sweden. From 1911 to 1925 nearly all of the operations of this type were done in the Scandinavian countries and the procedure was neglected by surgeons in other countries. While there had been 150 cases in Scandinavia up to 1927, there had been less than twenty reported in the United States, Canada and Eng-

land. Since that time there have been many successful operations with the Scandinavian figures of 382 embolic operations leading all the others.

While an occasional patient will survive without the removal of the embolus, we believe embolectomy is indicated in every instance when the diagnosis is made. We base this on the fact that we have been able to remove not only the embolus, but the accompanying thrombus in a high percentage of patients if seen within a reasonable time. Conservative measures advocated, such as the suction pressure boot, may play a part occasionally. Our experience has been that many of the patients who survived without operation did not have true embolisms, but rather arterial thromboses or the final closure of a vessel previously constricted by arterial disease, the previous constriction permitting and stimulating adequate collateral development. We have seen patients develop gangrene and eventually die with a suction pressure apparatus and in one patient the entire epidermis sloughed during such a treatment.

Surgical Technique: Local anesthesia should be employed exclusively and adrenalin, a severe vasoconstrictor, should not be added. These people are in poor condition and a general or spinal anesthetic is often too great a load for their circulatory system. Gentleness is of the utmost importance in this procedure. The incision is made over the femoral canal, just below the inguinal ligament for femoral, aortic or iliac embolus, and a vertical incision gives the best exposure. The femoral artery is isolated in the wound and a tape passed around either end of the exposed artery. A fine silk stay suture is placed at either end and a longitudinal incision made in the artery. If a thrombus is present, it is teased out with a smooth forceps from the distal end first. With a soft rubber catheter preventing the passage of clots below the incision, the proximal end is then removed. Frequently the thrombus breaks away from the embolus, which remains attached in the lumen. A wire corkscrew instrument may be inserted up the artery to dislodge the embolus. In order to protect the intima, it has been my practice to protect the corkscrew by a rubber catheter as it is introduced. The catheter may be withdrawn when the obstruction is reached. Usually the embolus begins to pass when the corkscrew is withdrawn, but no one instrument is always successful and some ingenuity is necessary. Suction applied to rubber or ureteral catheters may be effective in loosening the clot and on occasion we have borrowed many instruments from the urological and bronchoscopic departments, including the minute biopsy and flexible

foreign body instruments. In the femoral area it is advisable to expose the profunda to be sure its function is not impaired. The technique must be adjusted according to the pathology present. In one instance, Carter[1] was able to guide a femoral embolus into a profunda branch manually, thus reëstablishing the femoral circulation without the necessity of entering the arterial lumen. There must be free flowing, spurting blood, and when this does not occur, it indicates that there is still some obstruction and further efforts must be made to free the artery. In some cases incision can be continued through the inguinal ligament and the hand passed retroperitoneally along the large vessels to the bifurcation, and the vessel milked manually. Considerable blood spurting should be permitted to be sure that all fragments and clots have been removed.

In the presence of bilateral symptoms both femoral arteries are exposed at once. By lightly constricting the artery of the other side below the incision site, the possible passage of a clot into the opposite periphery can be prevented. For the same reason, even when only one side is involved, the pulsation of the foot on the unaffected side should be watched most carefully after the clot has been removed.

The artery is closed with fine arterial silk on minute curved needles, the sutures being placed so they do not enter the intima. Oversuturing should be guarded against. One should remember that the pressure at any point in the arterial wall is inversely proportional to the velocity of the blood flow and that a single running suture is often sufficient to prevent bleeding. Carrel and Key advocated coating sutures, needles and instruments with vaseline, but this technique has been found cumbersome and unnecessary. The needles slip and the delicacy of technique required for this type of surgery is too often sacrificed.

Irrigation of the artery with 25 per cent heparin solution at the time of operation is a recent addition to the technique. It seems to be helpful and probably has prevented formation of some immediate thromboses.

After Care:

1. *Heparin:* Heparinization is a definite adjunct to arterial surgery. It should be used routinely after operation. One must temper the continuous drip technique with patients whose cardiac status would not stand the continuous overloading of the venous system. In those cases, the clotting level may be maintained below normal by 5 cc. given every two or three hours. Dicoumarin, presented and discussed by Dr. Irving

S. Wright, at this same meeting, no doubt will play its part in making arterial surgery safer in the future.

2. Perivertebral sympathetic nerve block: Perivertebral nerve block after embolectomy is important. With the removal of the embolus and accompanying thrombus, the introduction of 5 cc. of 2 per cent novocaine into each of the lower dorsal and lumbar sympathetic ganglia relaxes the spasm and stimulates circulation, not only in the major vessels, but in the collateral circulation.

3. Care of the limb: The limb should be protected from bruising or skin breaks and should be kept warm, but not burned. It is best to wrap the foot in candy cotton and put it in a large cradle where the temperature is controlled between 88° and 94° F. Elevation of the leg is contraindicated but the oscillating bed with its gentle arterial massage, is helpful.

4. Drugs: After embolectomy the smooth muscle relaxers may play a part. Papaverine, atropine, and pantopon may be given as often as every two hours. Whiskey is also helpful at this stage.

5. Exercise: No effort should be made to make this leg carry weight until it has been shown that the circulation is intact. The cardiac status in most cases delays the attempt in walking until this prerequisite has been satisfied.

Should a second embolus occur it may also be removed. Cases have been reported in which as many as three consecutive embolectomies have been performed with recovery (Macfarlane). In a review of all the patients who were seen at the Post-Graduate Hospital between 1930-39, the difficulties of the differential diagnosis between embolus and thrombosis were observed. Rejecting certain doubtful cases in which the cardiac status was considered primary, twenty-six patients were described, of which twelve were operated and five survived—a percentage of 41.6 per cent. Of those who survived without operation, all lost their limbs. Again, the possible error in diagnosis of many of this latter group must be emphasized. Personal observations have been made on sixteen patients with true emboli, twelve of whom have been operated and four of whom were not operated. Dr. Franklin Carter, of the Post-Graduate Hospital, has had seven such patients, several of whom I have also observed. Of the total patients operated, thirteen have had the circulation restored. While the percentage of patients living today after this procedure is only 23 per cent, this figure can not be taken as a

true one for embolectomy success. It is actually 61.5 per cent, because it must be recognized that if embolectomy restores circulation it has been successful. Embolectomy can not be expected to prevent death from an advanced heart lesion or to prevent other phenomena. These patients die from the lesion causing the embolus, not from the embolectomy. If embolectomy is not performed, the death rate is higher from the gangrene which they usually develop or from the operation for the gangrene. This has been proved by many workers. I observed five patients who were not operated on, who developed gangrene and died. If such patients do have spontaneous recoveries, without operation, they are permanent vascular cripples. One such patient seen in the clinic recently recovered spontaneously, but now has zero oscillometric readings and such inadequate collaterals that amputation seems almost inevitable. One should not be discouraged by the low percentage of patients living five years after their operation. Were this same outlook carried to the field of cancer or brain surgery, many patients now cured of these lesions would be dead.

The end results in the embolectomies in Sweden showed that one quarter die in one year, one-half are dead in three years, one-third are alive in five years and one-eighth are alive in ten years. The graph is practically identical with that of those living after excellent surgical and x-ray therapy for cancer of the breast. This seems sufficient answer to those surgeons who have stated that the operation is useless, because of the poor risk of the patient group. Certainly no one would advise against operation for cancer of the breast merely because only one-eighth of the patients will survive ten years.

One of our patients operated sixty hours after a large saddle embolus of the abdominal aorta had been lodged, is alive today with complete circulation in one limb and in the other limb to the knee. This patient was operated on, at the instance of the family, in a condition of extremis, with a temperature of 104°. It was their contention that the patient who was a minister, would survive the procedure because of his profession, if given surgical help. Emboli from both sides were removed with considerable difficulty with restoration of circulation in one leg and improvement of circulation in the leg which was already gangrenous to the middle of the calf. This is illustrative of the factor so well outlined by the late Osler, whose precept of never letting a person die of one disease merely because he has another, is frequently forgotten by us today.

The recovery of this patient and other less dramatic recoveries have convinced us that no arbitrary time limit, as to whether to operate or not, can be placed on these patients. It is our intention to operate on all of them as soon as we see them and we believe that more people with emboli will be alive in the next ten years than have survived in the past.

II. Aneurysm

Diagnosis, symptoms and treatments of peripheral aneurysms vary greatly with their site and, because of that, only general therapeutic suggestions can be given. While we define aneurysm as a sac filled with blood communicating with an artery, its subdivisions, as contained in the text books, number twenty-five. For clarity I will subdivide the peripheral aneurysms as follows:

Peripheral Aneurysm
- *I. Arterial*
  - Acquired
    1. Result of trauma
    2. Result of degenerative disease
  - Congenital
- *II. Arteriovenous*
  - Acquired
    1. Result of trauma
    2. Result of degenerative disease
  - Congenital

I. Arterial Aneurysm: In arterial aneurysm we have a weakness of the wall of the vessel due either to an increased arterial pressure or a traumatic or degenerative lesion of the vessel wall or a combination of both of these factors. The sac which develops has a neck through which it communicates with the main vessel and the contents of the sac are liquid and coagulated blood in various stages of resolution. The wall of the sac will be of the so-called true or false aneurysmal type. In the former the weakened arterial walls are pushed ahead by the dilatation and in the latter, the walls of the vessel are destroyed and the sac is made up of surrounding tissues with only an endothelial lining. There may be efforts to strengthen the wall by the proliferation of fibroconnective tissue in either of these forms, but this fails eventually because of the force of the blood which at times is sufficiently strong

to erode cartilage and bone. The clots are white at the periphery and red at the center with many degenerative changes occurring in them. The older ones become calcified.

Symptoms: While all aneurysms form a *tumor*, the contiguous structure, particularly where the aneurysm is small, may hide it. An *expansile pulsation* is present in the early aneurysm, but with further clot elimination, the pulsation may be transmitted or even obliterated. *Pain* is a variable symptom, depending upon the structure which is being compressed by the growing tumor. In the extremities this may be a negligible factor, although in the popliteal aneurysms pain and weakness of the muscles supplied by the sural nerve may be an early sign. The *pulse* is weak or absent distal to the aneurysm. This applies also to the oscillometric readings and blood pressure. Paré's bruit, which is present in early cases, depends on the clotting. When present, it is of the rough systolic type. In addition, in the acquired type there will be a scar at the site of injury. The congenital aneurysms at times are multiple.

Treatment: 1. The ideal treatment of either acquired or congenital aneurysms is excision and end-to-end anastomosis of the vessel. This is more often possible in the traumatic type than is generally supposed. We have performed this operation successfully four times in the last year. The artery is exposed, the aneurysm excised and the arterial ends sutured with interrupted and continuous fine arterial silk, after which the suture line is reënforced with nearby muscle or fascia. By release of the vessel from its bed and flexion of the joint a defect of 4 to 5 cm. may be closed. This point can not be overstressed in war surgery, where laceration or division of an artery is frequently considered sufficient cause for the amputation of the involved extremity.

2. Obliterative Operative Procedures: The reapplication by Matas of the ancient conceptions of Philigrius of obliterating the involved vessel is the treatment of choice in many of these patients. The circulation is controlled above and below the aneurysm sac, the sac then widely opened, its contents of debris, clots and necrotic material evacuated and each collateral opening into the sac closed by sutures. The major arterial openings are ligated and then sutured from within. The sac is obliterated by multiple layers of sutures without excising the sac. A large muscle transplant aids in obliteration. In the popliteal space we have used the gastrocnemius and the popliteus muscles most successfully. In some of the smaller ones muscle transplants are not required. There is a good

deal of misconception about the principles of this operation even in the minds of well trained surgeons. The principle is to obliterate, *not remove,* the sac. To remove the sac one must do irreparable damage to the extremity. Excision of an aneurysm of this type frequently results in gangrene.

3. The most successful type of reconstructive operation on the artery is the use of a vein transplant. A rather large vein must be selected and sutured to the ends of the artery to bridge the defect. The incidence of thrombosis, which so frequently attends such an operation, can be decreased by heparin and Murray has shown many well functioning vein transplants years after their introduction. Babcock[2, 3] in his carotid jugular anastomoses, demonstrated how well a vein can accommodate the arterial blood. The large jugular vein, when united to the smaller carotid artery, shrinks down to the size of the arterial column, and after a time its wall becomes as thickened as the artery. This operation will have its place many times in the repair of the injuries resulting from the present world conflict.

4. The modifications of the original Matas[4] procedure of opening the aneurysm and plastically repairing the wall over a tube or other foreign material has been accomplished in selected instances, but an arterial wall once so seriously damaged as to stretch into an aneurysm may weaken again. The use of an absorbable material over which to suture, such as glucose, is of only experimental interest at the present time. Experiments are likewise being made with the use of other foreign matter such as talcum powder and cellophane which cause peri- and endoarteritis. It has been shown that these and other similar materials cause inflammation and fibrosis to a marked degree and it may be possible to take therapeutic advantage of this fact. One operation of this type has recently been performed by us.

In any type of treatent of aneurysm where the main vessel is or may be occluded, it is most important that stimulation of collateral circulation be continued. Antispasmodic drugs, whiskey, external heat and avoidance of all trauma are all valuable agents. Lumbar sympathetic nerve block has its place in relaxing spasm. All strain on the part must be avoided until there is proof that adequate circulation is established and in cases where the small collaterals are carrying the circulation the patient must be restricted physically within the limits of his arterial supply.

II. Arteriovenous Aneurysm:

Acquired Arteriovenous Fistula: The most common cause for the acquired type of arteriovenous aneurysm is gun shot, stab or airplane and automobile injuries. A large percentage of them follow war wounds. The arterial blood rushing into the sac or vein causes definite physiological changes. They are as follows:

Physiological Changes Following Arteriovenous Fistula

1. A blood pressure fall with recovery, but greater pulse pressure
2. An increased pulse rate.
3. An increased venous pressure
4. Increased cardiac output (depends on size and location)
5. Temporary decrease in size of heart and artery, then dilation with hypertrophy of the heart
6. Increased total blood volume
7. Collateral circulation around fistula

The degree to which these changes occur depends upon the size of the vessel involved and the length of time the abnormal communication has persisted. If the communication is at all large, its closure is imperative to prevent changes and eventually the cardiac failure which results. The symptoms in the acquired type of aneurysm are usually so apparent that diagnosis is evident. The scar at the site of the injury, followed by enlargement, dilation of the veins of that extremity, increased temperature and a bruit are confirmatory. The Paré sign of decreased pulse rate with pressure over the fistula will be present, as will a diminished pulse and blood pressure and oscillometric readings distal to the fistula. An arteriogram is confirmatory. Pain depends upon the extent of the pressure on the nerve or sensitive parts. All symptoms following venous congestion, such as pigmentation, dermatitis, ulceration, edema, hemorrhage or even gangrene may be present. A higher oxygen content in these veins than in the normal vein, due to the arterial flow is another confirmatory test.

Pathology: The connection is lined by endothelium and at times clots develop in the sac. The venous blood, driven back by arterial pressure during systole, may enter the artery during diastole. Arterial blood returns through the nearest venous channels and starvation of the periphery may result.

Surgical Treatment: It is wise to postpone operation until four to

six months after the development of the fistula to permit the sudden physiological changes accompanying the fistula to have reached a level and, more important, to permit collateral circulation to become adequate. At the time of the repair, the physiological changes previously mentioned must be considered, as the closure of the fistula causes an exact reverse of all the points mentioned. If the fistula has been present for a long time, it may be necessary first to decrease the blood volume by phlebotomy to prevent overstrain of the cardiovascular system. It is preferable to omit the tourniquet when the operation is performed. No one operative procedure can be used for all types of fistulas. The ideal treatment would be one in which the fistulous communication was closed and the continuity of the vessels reëstablished, but unfortunately this is rarely possible. The site of the anastomosis should be exposed and explored and tapes applied above and below the fistula. The closing of the upper tape will not result in circulatory failure distally in those cases where the collateral circulation is adequate. Care must be taken to ascertain this at the time of operation. The type of operation to be selected may be one of the following:

1. Repair of the fistula in the arterial wall, through the opened and sacrificed vein. Suture materials should be of the finest arterial silk on non-traumatizing, minute, round needles, such as are used in eye surgery. These sutures should not enter the intima. A section of near-by fascia or muscle makes a better reënforcement than the fistulous sac or vein. The ligation of the vein in these instances appears to be of therapeutic value, compensating for the reduced arterial supply by decreasing the rapidity of the blood return.
2. Ligation, proximally and distally, of the artery and the vein, with excision of the intervening fistula and vessels is frequently the treatment of choice, where collaterals are adequate. In this type of treatment the intervening vessels must be removed or the fistula may recur. This operation is used most often in the upper extremity, head or neck.
3. In some cases it is impossible to remove the fistula, because of possible damage to secondary circulation. Quadrilateral ligation is then performed. The fistulous tract is opened and the clots evacuated, all openings into the fistulous tract closed by fine arterial sutures and the sac obliterated by muscle transplant, imbri-

cation and plication. The use of this operative principle has saved many limbs which in previous years it would have been necessary to sacrifice.

Congenital Arteriovenous Fistula: Many of the symptoms and signs, as well as the therapeutic measures detailed for the acquired aneurysm apply to the congenital type. In the treatment of congenital arteriovenous aneurysm, however, the cardinal point to remember is that they are usually multiple. All of these multiple connections may not be open and functioning at the same time. This point should be explained to the patient, since multiple operations may be required as a result of this. The etiology of these congenital arteriovenous communications is still under investigation. Arteries and veins anastomose most frequently in the hands, feet and sexual organs, as shown by Hoyer, Krogh and others. In studying the embryological rests frequently demonstrated in the newborn, it is not difficult to conceive of the same failure of closure in the arteriovenous system. They are usually multiple and are found most frequently in the upper extremities. When they appear in the lower extremities, they are often diagnosed as varicose veins with onset first noticed at three to five years of age. The history discloses that the physician consulted at that time advised that nothing be done, as the patient "might grow out of it." Another form of arteriovenous connection is the so-called aneurysmal varix, in which the enlarged varicose veins connect with an artery. This lesion, by no means rare, is also commonly diagnosed and treated as varicose veins with resultant technical complications. The *symptoms* in these congenital type lesions differ with the number, size, duration and position of the communications. Large ones are particularly frequent in the upper extremities, while minute ones may occur on the face, particularly around the eyes and mouth, where the term pulsating hemangioma is applied. A congenital fistula was seen in the neck of a patient of Dr. Irving S. Wright[5] in which a mass of vessels in the suprahyoid muscle area was fed by the left lingual, external maxillary and inferior thyroid arteries and so many abnormal connections from the right external carotid that it was necessary to extirpate all of the main branches of the left external carotid and the entire right external carotid artery in order to close the fistula. Signs of *thrill* and *bruit* at the site of the fistula and arterial blood in the veins are diagnostic in this type of lesion, as they are in the acquired type of fistula, except that in the congenital fistula they are usually larger.

Treatment: The treatment of the congenital fistulas varies with their size. Many small ones, particularly on the face, may be surgically excised and some of the ones which have been sclerosed with a small amount of solution have never recurred. Radium has helped a few. In treating the large congenital fistulas one must be prepared for an extensive and, many times, a multiple procedure. This multiplicity can not be overemphasized. The operations are best performed without a tourniquet so that the site of bruits can be determined and each one eliminated. The operation of choice in the large lesions is quadrilateral ligation and excision of the arteries and veins involved. At times one must remove vessels which appear necessary to the life of the part, but collateral circulation is present so frequently that most of these limbs will not be lost.

The tendency of these fistulas to invade and spread like malignancies has been noticed, particularly in one of our patients. Matas has reported cases which appeared to metastasize. Amputation in some instances is necessary and indicated. In some of these patients connections closed at the time of the operation will open with the increased arterial pressure. In one instance we closed eleven communications only to have the patient return the following year with five new ones. One must be prepared for such discouraging results and continue with the operations in stages until cure is achieved. While local relief is hoped for, it is to prevent the eventual cardiac collapse that the operation is performed.

REFERENCES

1. Carter, R. F. *Personal communications.*
2. Babcock, W. W. *Text-book of surgery.* 2. ed. Philadelphia, Saunders, 1935.
3. Babcock, W. W. *Personal communications.*
4. Matas, R. Personal experiences in vascular-surgery; a statistical synopsis, *Ann. Surg.*, 1940, *112*:802.
5. Wright, I. S. *Personal communications.*

TESTICULAR BIOPSY IN THE DIAGNOSIS AND TREATMENT OF STERILITY IN THE MALE*

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THE persistent absence of spermatozoa from the semen denotes absolute sterility in the male. This condition requires that either no substantial number of spermatozoa is being formed, or that an obstruction or defect exists which prevents the escape of the cells from the seminal tract. Certain clinical guides are helpful in determining which factor is the cause. Thickened epididymes favor occlusion, while atrophic testicles indicate that the germinal epithelium is deficient. It has become increasingly apparent, however, that azoospermia may be associated with genitalia which are normal to external examination. Accordingly, there is a real need for an accurate way to determine whether the lack of spermatozoa is due to aspermatogenesis or occlusion. A correct diagnosis is obviously essential to proper management, for an occlusion calls for reëstablishment of the patency of the ductal systems, whereas incomplete spermatogenesis theoretically demands that some agent or set of agents be supplied to motivate spermatogenesis.

It has been said that one good diagnosis is worth ten haphazard treatments. The use of testicular biopsies bears out this adage in the problem of the sterile man. The study of testicular tissue has proven to be a reliable and practical method in accounting for the absence of sperm in the semen, and promises to minimize errors in treatment.[1] The tissue likewise affords a new source of information relative to the histopathology of the human testes and may assist in clarifying some of the fundamental clinical concepts of seminal deficiencies.

The procedure of obtaining the biopsy requires no special skill and entails little discomfort and incapacitation. The genitalia are prepared for operation and a small area in the scrotal skin is anesthetized with

* Presented December 4, 1941, before the Stated Meeting of The New York Academy of Medicine. From the Department of Surgery (Urology) of the New York Hospital and Cornell University Medical College.

1 per cent novocaine. An incision is made and carried down through the tunica vaginalis. A pair of ocular palpebral retractors is inserted, and the tunical albuginea is exposed. A small "V" shaped incision is made therein and a minute piece of testicular tissue is excised. Silk or fine plain gut sutures are used to arrest hemorrhage and approximate the layers of the wound. The operation is repeated on the opposite side. A suspensory is applied and the patient is sent home from the operating room. The tissue is fixed in Bouin's solution and sections are prepared in the usual manner.

Two main classes of testicular tissue are found.[2] The seminiferous tubules may contain either normal or defective germinal epithelium. The degree of cellular activity varies considerably in different tubules in each section, but the general contrast is striking and offers little chance for serious confusion. Several types of defective germinal tissue may be seen. The biopsy specimens from some men with normal sized testicles exhibit spermatic cells which have progressed to the spermatid stage, just short of full maturity. Others have germinal epithelium which is arrested at an early stage of spermatogenesis. A third type have tubules almost devoid of germinal epithelium, and their lumens may be filled with hyaline. A fourth type of abnormal testes is characterized by extraordinary proliferation of fibrous tissue about the tubules. Sections of testes associated with occlusion of the efferent seminal tracts have, in main, well-organized germinal epithelium with many mature spermatozoa.

The clinical usefulness of the biopsies is quite apparent. Active normal spermatogenesis requires no stimulating agents. Complete degeneration of the germinal tissue defies treatment with substances now available. Thus, useless or misapplied therapy is avoided and an approach to rational treatment is made.

The mandates of successful treatment of sterility, however, include more than a mere consideration of the histopathology of the testes. Three essential criteria are involved. They are:

1. The primary cause of the disturbance must be recognized and evaluated.
2. Specific and potent therapeutic agents must be available and assimilable.
3. The end organ must be refractory.

Lack of knowledge of certain important facts concerned with these

three criteria accounts for the generally unsatisfactory state of therapy at this time. It may be appropriate to examine these principles in the light of present developments to evaluate current and future modes of the clinical treatment of impaired fertility.

It is likely that faulty spermatogenesis can be assigned as due to one of four causes. The identity of the particular cause is probably the key to effective therapy.

1. An inherited gametogenic factor may account for sterility in man. As yet there is no clinical proof of this theoretical possibility, but other species furnish notorious examples of this genetic phenomena. The mule, which is a hybrid animal, is always sterile. There is no possibility of revoking chromosome patterns, and treatment is futile.

2. A second cause of spermatogenic failure may be some deficiency disease. This is clearly indicated by the effect of inadequate diets in experimental animals.[3] The work of Dr. John MacLeod[4] has demonstrated the necessity of certain foodstuffs, enzymes, and vitamins to the life processes of spermatozoa. The needs of the germinal epithelium may not be dissimilar to the requirements of sperm.

Subclinical or mild deficiency states are now recognized as established clinical entities, and subsequent investigations may reveal that defective spermatogenesis is linked with an inadequate vitamin supply or, more likely, to a failure to absorb and utilize these and other substances.[5, 6] The past and present clinical experience with corrective dietary regimes and vitamin medications have not been singularly encouraging. Future advances may reverse present attitudes, and it is possible that certain cases of infertility due to deficiencies will be corrected and cured.

3. There is no doubt that the gonads are intimately linked with the other glands of the endocrine system.[7] Nearly thirty years ago it was shown that removal of the pituitary caused prompt atrophy of the germinal epithelium. Since then an enormous amount of interest has been displayed in the relationship of the reproductive glands to the other endocrines. The clinical application of endocrine therapy in man has borne far less brilliant results than some of the experimental animal work. There are a number of well authenticated reports which illustrate effective treatment of impaired fertility in men with endocrine products but the failures are far more common than the successes. The deserving skepticism is well understood when it is realized what great

obstacles still remain in therapeutic pathways. Species vary greatly in their responses to endocrine substances so that much of the experimental work on animals and birds cannot directly be transferred to the human with the assumption that it is applicable. We have no simple tests to evaluate or diagnose subclinical or minor grades of endocrinal disorders. The therapeutic products which are available are not specific and probably far below basic requirements of actual need. These and many related problems await clarification before the dreams of a "specific hormone" for spermatic tissue will be available in the same sense that insulin is used for diabetes.

4. A fourth class of disturbances which may alter spermatogenesis may be grouped under the term "constitutional and local disorders." It is evident that the testicles are labile structures and are sensitive to certain generalized alterations of body function. It is known that debilitating illnesses will arrest spermatogenesis. Artificially induced fever will cause transient injury to the germinal layers.[8] Much speculation is given to the effect of less definite influences such as fatigue, nerve strain, overwork, alcohol and minor illness. It may well be that subnormal semen is much more adversely affected by these factors than are specimens of high quality. These agents may then resolve themselves into individual considerations which have relatively little effect on the very fertile, yet are especially harmful to those less generously endowed. The various diseases of the genitalia are adequately described in text books and the influences on fertility are well known. The biopsies of testicular tissue have revealed, in some instances, marked thickening of the fibrous tissue encircling the seminiferous tubules. An explanation for this is not ventured herewith, but it is conceivable that these deposits may act as barriers and prevent proper nourishment of the germinal epithelium. This affords a probable example of a non-refractory end organ incapable of being stimulated.

No claim is made that the examination of the biopsied testicular tissue will depict which one of these foregoing conditions has caused aspermatogenesis. The inconsistent results of treatment are more fully appreciated, for response depends on: the identification of the cause, the use of appropriate corrective agents, and the ability of the testes to respond to such stimulation. Testicular biopsies will not solve all these problems, but will obviate some of the difficulties. The information gained from the biopsy will certainly prevent some men from re-

ceiving innumerable injections of hormones when the testes are proven to harbor large numbers of spermatozoa, or are atrophic to a hopeless degree. A selection of favorable cases for treatment is made possible and a reasonable trial is given to substances purported to have therapeutic value.

Occlusions in the seminal passageways, as well as faulty spermatogenesis, may cause absolute sterility in men. The majority of acquired obstructions are located in the lower portions of the epididymes or beginning of the vasa. Two cases of congenital absence of the vasa have come under my care during the past two years. Notwithstanding the fact that a normal outlet for spermatozoa had never been available, the testicular biopsies demonstrated fairly normal spermatogenesis. The ability of the testicles to maintain their function despite years of obstruction is in harmony with the theories that the epididymes are capable of absorbing and disposing of spermatozoa. These organs, rather than the seminal vesicles, are perhaps the true "graveyards of the spermatozoa." This cyclic process of production and absorption may account for the entire absence of sperm in the semen even though a few mature sperm are seen in some biopsies showing faulty and poor spermatogenesis.

Clear indication for operation is afforded by the aid of biopsies. An obstruction or congenital anomaly of the efferent tract is to be inferred if several ejaculates have no sperm yet the biopsy shows well-differentiated germinal epithelium with many mature spermatozoa.

A second operation is then performed and a full exposure of the scrotal contents is obtained. The patency of the vas is tested by injecting a fluid into its lumen at a level with the body of the epididymis. The epididymis is punctured at a corresponding point and the expressed secretions are examined immediately for sperm. If the vas is patent and sperm are found a union of the two structures is formed after the method which Martin described forty years ago. Arterial silk sutures serve as excellent material for the juncture of vaso-epididymal anastomosis. If patency is established, sperm will appear in the ejaculate within 12 months. Failures are due to inability to complete the operation because of extensive obstructions along the vas, or subsequent postoperative closure of the fenestra between the vas and epididymis. The operation may also fail to bring clinical results for, although at least one tract has been opened, too few or immotile sperm are ultimately secured in the semen. Successful results should reach about 20 per cent of those operated

upon, and yet the failures are no worse off than prior to operation. In retrospect, it may be said that all too often such men are dismissed as hopeless and that, if they are willing to accept unfavorable odds, the operation deserves trial.

Summary

External examination of the male genitalia does not always indicate the state of spermatogenesis or condition of the epididymes and vasa. Testicular biopsy is a practical method of appraising the value of the spermatic tissue. Appropriate treatment can be applied and useless therapy avoided. The inconsistent results of treatment of grave disorders of the germinal epithelium are commensurate with the existing etiological and therapeutic problems, but future research promises much for the development of efficient treatment.*

REFERENCES

1. Charny, C. W. Testicular biopsy; its value in male sterility, *J.A.M.A.*, 1940, *115:*1429.
2. Bothe, A. E. and Robinson, E. K. Histological study of testicles in 100 autopsies, *J. Urol.*, 1933, *29:*425.
3. Mason, K. E. Specificity of vitamin E for testes, *J. Exper. Zool.*, 1930, *55:* 101.
4. MacLeod, J. The effect of glycosis inhibitors and certain substrates on metabolism and motility of human spermatozoa, *Endocrinology*, 1941, *29:*583.
5. Mulinos, M. G. and Pomerantz, L. Reproductive organs in malnutrition, *Endocrinology*, 1941, *29:*267.
6. Reynolds, E. and Macomber, D. Defective diet as cause of sterility, *J.A.M.A.*, 1921, *77:*169.
7. McCullagh, E. P. and Ryan, E. J. Spermatogenesis, *J. Clin. Endocrinol.*, 1941, *1:*728.
8. MacLeod, J. and Hotchkiss, R. S. Effect of hyperpyrexia upon spermatozoa counts in men, *Endocrinology*, 1941, *28:*780.

* Six case histories with microphotographs, illustrating the usefulness of testicular biopsies, were included in the original presentation of this paper.

THE EPIDEMIC CONSTITUTION IN HISTORIC PERSPECTIVE*

IAGO GALDSTON

"SCIENTIFIC epidemiology . . . began like almost everything which makes life worth living, in Ancient Greece." (Major Greenwood) In the books of Hippocrates entitled *Airs-Waters-Places,* and *Epidemics I-III,* we have the beginnings of epidemiology. The first is an essay, which exhorts the physician to appreciate the influence of environment, season, and mode of life, on health and disease. The second, *Epidemics I-III,* offers, in a sense, case notes to illustrate the propositions expounded in *Airs-Waters-Places.*

There are critics who find fault with these books, for in them, intermingled with the astute epidemiological observations, are to be found comments on critical days, on coctions, crisis, and crasis, and these they find repugnant. But such critics are rather superficial for in their objections to particular details they lose sight of the basic thought. That which entitles Hippocrates to be considered the founder of scientific epidemiology is not his speculations on the origin of the Scythians' impotence, nor his theory on the critical days, but is rather an understanding vast and profound. That understanding is of man's relationship to his universe both immediate and remote. This appreciation is leavened in all the genuine works of Hippocrates. It is the compelling warrant for his rejection of the supernatural or deistic origin of disease. It illuminates and rationalizes his therapeutic practices. It holds within the bounds of sense and reason his diagnoses, his prognosis, and his nosography. It accounts for his dependence on nature to effect the cure. But his deeply philosophical appreciation of man's relationship, and of man's susceptibility in health and disease to the interplay of the forces in his environment is best revealed in Hippocrates' epidemiological books. These books, as Jones observes, are without pretensions to literary form, but they constitute "the most remarkable product of Greek science" (W. H. S. Jones, *Hippocrates,* Vol. I, p. 141). Their

* Delivered December 31, 1941 before the History of Science Society Meeting, in association with The American Historical Association, Chicago, Illinois.

distinction lies less in what is expressed than in what is implied in their texts. These books are the products of maturity, the yield extracted by time and much meditation from a vast and varied experience. In these works Hippocrates advances the simple thought that man's private ills are chiefly the result of his own ignorance and of his slovenliness, but the epidemic diseases are the resultant of inimical forces, of disequilibria in man's environment. In *Airs-Waters-Places* Hippocrates expresses the dictum that he who wishes to pursue properly the science of medicine must consider the effects of seasons, winds, the properties of waters, those of the soil, and "the mode of life also of the inhabitants that is pleasing to them, whether they are heavy drinkers, taking lunch, and inactive, or athletic, industrious, eating much and drinking little." (W. H. S. Jones, *Hippocrates,* Vol. I, p. 71-72). There is revealed in this short passage a wealth of insight, the penetrating appreciation of man's position in the intricate web of Nature.

It is an easy yet pardonable fault to read into the writings of Hippocrates more than he ever knew or intended, and to credit him with wisdom and knowledge born in later years. Our evaluation of the Hippocratic writings on epidemic diseases, however, is free of these faults. It were difficult rather to prize them excessively, for they are unique and stand alone for many ages. There is nothing in what has come down to us from the ancient medical writings that even remotely suggests that in these matters there had been a forerunner to Hippocrates.

Nothing in the speculations of the contemporary philosophers corresponds to the basic idea propounded in the Hippocratic writings on epidemiology.* On the contrary, Hippocrates, in the book *Nature of Man,* shows scant respect for the theories and speculations of the philosophers.

Hippocrates was a naturalist who in the mosaic of life counted man as a creature bound with all the rest in the common matrix of earthly forces. Four hundred years later the Latin poet Lucretius (95-52 B.C.) eloquently, though somewhat mordantly, espoused a similar naturalism.

In *Epidemics,* which I have characterized as case history illustrations of the thesis of *Airs-Waters-Places,* we come upon the Greek term κατασταση derived from κατασταμα and defined (Liddell & Scott) as "a state, situation, condition, constitution, quality."

* See in this connection: Fredrich, Carl, *Hippokratische Untersuchungen,* Berlin, Weidmannsche Buchhandlung, 1899, p. 130, p. 162.

In the authoritative translations of Hippocrates *katastasis* is rendered as "constitution." It is well for us to note this term, for about it revolves much of later epidemiological thought—and I may add, confusion. In the Hippocratic works *katastasis* connotes environmental factors contributing to the engenderment of epidemic diseases. In later times, the term *katastasis* was sheared of its Hippocratic meanings, and while commonly employed, was assigned a variety of meanings. We will return to the *katastasis*, or more specifically to the epidemic constitution, later. To sustain the thread of our story we need to trace further the history of epidemiological thought. But trace is hardly the fitting word; we rather march with seven league boots over a stretch of some thirteen hundred years.

The revival of epidemiology is to be credited to the French physician Gulielmus Ballonius, and to Thomas Sydenham. Ballonius was the earlier of the two. He was born in Paris in 1538 and died in 1616, having attained to the age of seventy-eight. Sydenham was born eight years after the death of Ballonius, that is in 1624. Ballonius carried on in the best Hippocratic tradition—to observe, to report, to reflect. In his *Epidemiorum et Ephemeridum*, published after his death by his nephew, in 1640, Ballonius follows the pattern of Hippocrates. He gives the *katastasis* of the years, and then reports the cases he had seen. We have in these works a catalogue of clinical records. But we have here little else. Ballonius follows the pattern but adds nothing to the knowledge proffered by Hippocrates. It is quite otherwise with Sydenham. He too returned to Hippocrates, but he went further than Ballonius in the pursuit of the problems of epidemiology. His epidemiological writings offer us no clinical case records, such as those of Ballonius afford, but they do tease the heart of the matter, the epidemic *katastasis* —or, in Sydenham's words, the epidemic constitution.

It is not possible in this discursive review of the history of epidemiology to expound minutely, to so-to-say comb, spin and reweave the fabric of Sydenham's thoughts on epidemiology. Moreover, that has been done exceedingly well by Major Greenwood. I will rather borrow and adopt Greenwood's lucid summation of Sydenham's epidemic constitution.

> "The complete morbid process of an epidemic disease is made up of two parts; the first is specific (the a, b, c, &c., of the formula), subject to secular modification and also to short period oscillations—

i.e., it is a doubly periodic function of the time. The second part is generic, common to all species of epidemic diseases and a function of some terrestrial conditions included under the term "Epidemic Constitution."*

It is this second part, the generic component of the epidemic constitution, defined not exclusively in terms of atmospheric conditions but rather as "a function of some terrestrial conditions" which constitutes Sydenham's most valuable contribution to epidemiological thought.

Sydenham's works on epidemiology gave impetus to the study of the subject but what followed was not in the order of the original. The later works are lacking in philosophical insight, in breadth of understanding. They are provincial rather than catholic. They are painstaking, and scrupulous collections of meteorological data. They are inspired by the vain hope that the secret of epidemic diseases could be wrested from the collected data on barometric pressures, temperatures, humidities, wind directions and velocities, and rainfall. In the two volume edition of Sydenham's collected works published by the Brothers de Tournes in Geneva, 1736, there are included twenty-one contributions on epidemiology from the pens of twenty authors. Among them we find the illustrious Ramazzini. These contributions are uniformly devoted to reports on climatic conditions prevailing in given localities during given periods of time, and to notations on the diseases current during those periods and in those locations.

To catalogue the different authors who attributed epidemic diseases to the depraved constitutions of the atmosphere, listing their individual and differing opinions on the source of the atmospheric corruption were a large and profitless task. It is more profitable to abstract from this enormous mass of published opinion, theory, and notation, its common factors, for we can thus identify the vis a tergo that motivated and directed the thinking and labors of these men. To achieve this we must rise above the particulars to survey the broad terrain.

It is patent that the time span of two thousand years, covered thus far in our review, embraces three epochs in thought on epidemic diseases. These we may designate as the epochs of Hippocrates, of Sydenham, and of the climatological epidemiology.

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* Major Greenwood: Sydenham as an epidemiologist, *Proc. Roy. Soc. Med.*, London, 1919, Epidem, Sect., vol. XII, Part II.

We have dealt at length with the Hippocratic epoch, but less amply with the other two. To appreciate what with some broad license I term the phenomenon of Sydenham, we need to grasp clearly the temper and spirit of his age. During Sydenham's lifetime the medical renaissance initiated by Thomas Linacre (1460-1524), the "restorer of learning" in England and first president of The Royal College of Physicians, reached its culmination. Sydenham was the last of the great English physicians who were nurtured in the ancient medical lore which the classical renaissance had resurrected and revivified.

Sydenham lived in the age of Shakespeare, Bacon, Milton and Dryden, of Galileo, Kepler, Descartes, Boyle and Newton, and of William Gilbert of Colchester, William Harvey of Folkestone, and John Locke of Wrington. But Sydenham did not fall under the even sway of all these greatest among English poets, philosophers and scientists. Thus, it does not appear that either Harvey, or Boyle, or Descartes, or Newton moulded his thinking. Sydenham was indeed, as his followers fittingly described him, the English Hippocrates. With Sydenham the Renaissance came to an end and the dawn of a new age was ushered in, the age of modern science, with its instruments of precision, and its inductive techniques.*

Thought was now on a new tangent. Man found anew his own "bright earth" and, himself. With consuming eagerness he set out to explore the microcosm. With the aid of his balances, his microscopes, his thermometers and barometers, his measuring rods and his chemical retorts he uncovered the wonders of the universe. A new enchantment was upon him, one that alienated him from his former devotions. It is this new enchantment, the limitless faith in inductive science, that accounts for so many men's eager scrutiny of the atmospheres for the secret of the epidemic diseases and for the conviction shared also by numerous others, that the noxious principle could be isolated from the complex of man's physico-chemical environment.

The *katastasis* of Hippocrates was for the while forgotten. But the study of epidemics continued, nay was pursued with even greater intensity. This study developed along three tangents: statistical, historical and bacteriological.

The statistical study was initiated by John Graunt, the son of a

* Within the lifetime of Sydenham, Harvey published *De Motu Cordis*, Descartes his *Méthode;* Boyle performed his revolutionary physico-mechanical experiments; Malpighi initiated his histological studies; Leuwenhoek discovered the protozoa; Hooke published his *Micrographia*, John Graunt drew up his *Bills of Mortality*, and Newton issued his *Principia*.

London draper, who himself became a prosperous shopkeeper and a Fellow of the Royal Society. In 1662 Graunt published a volume of statistical deductions based on the Bills of Mortality. He thus opened a new terrain which yielded to his followers most illuminating data on the dynamics not only of epidemic diseases but of a vast variety of other social and biological phenomena.

The history of epidemic diseases was, of course, of continuous interest to man, and was even intertwined in his chronicles with the tales of the fortunes of men and of states. Toward the end of the Eighteenth Century, however, the history of epidemic diseases was cultivated as a special discipline. The names of Philipp Gabriel Hensler, Leonhard L. Finke, Noah Webster, J. A. F. Ozanam, August Hirsch, J. F. C. Hecker, and Charles Creighton are preëminent in the history of epidemic diseases. Creighton's *A History of Epidemics in Britain* is without doubt the "capo lavoro" in this field. It is rich in scholarship, profound in understanding and enormously wealthy in factual data.

Before the influenza pandemic of 1918 swept the earth, most of the historical data on epidemics that had been gathered in the preceding centuries, was considered by most epidemiologists and physicians to be only so much curious lore by which to witness the blind gropings of the pre-bacteriological eras. However, the devastating influenza plague of 1917-1918 which dwarfed in its destructiveness the ravages of the World War, jolted at least a few among the epidemiologists out of their smug and patronizing state of mind. These epidemiologists rediscovered the precious worth of the historical studies on epidemics, and they have since made splendid use of the facts and ideas which these studies afford. The use that is lately made of the historical data will be dealt with later.

There remains to be mentioned the last of the three tangents of epidemiological development pursued since the days of Sydenham, namely, the bacteriological. The history of this development is too well and too commonly known to require elaboration. It need only be recalled that with the discovery of the disease-producing bacteria, epidemiology promptly became identified with bacteriology, so that the two were almost considered synonymous terms. Pettenkofer's was the last brave stand of the "constitutionalists" against the bacteriologists. Thereafter bacteriology held undisputed mastery over epidemiology. There were of course rebels, and heretics; but they were as voices in

the wilderness. Major Greenwood neatly sums up the situation in the following words:

> "It is true that some of the leaders of the victorious bacteriological army, including Koch himself, warned us that the discovery of parasites and the elucidation of their life histories left much of the mechanism of herd illness unexplained, but some of the commissioned officers and all the camp followers of the army would know nothing of this caution. It came to be believed, is still believed by a majority, that epidemiology, from the scientific point of view, is a mere appendix of bacteriology, that when the means of infection and the vehicles of infection have been identified, the problem of an outbreak of herd sickness is solved. All the ideas of the ancients were dismissed as archaeological lumber and the work of such writers as Farr, Brownlee, and Ross politely ignored, taken to be mathematical, and therefore intellectually respectable, but of no practical importance."*

Such was the state of epidemiology during the first decades of the present century. Such it is this very day for most medical men. Two departments share between them the whole terrain of epidemiology: one is the statistical department; the other, the bacteriological. During the last two decades, however, there has developed in the field of epidemiology a revival of interest in that which has for so long been forgotten and neglected—the *katastasis* of Hippocrates, the epidemic constitution of Sydenham—and this has come about in the most interesting and diverse of ways.

The precipitating cause of this revival was the last great influenza pandemic, but antecedent to it there were prodromal signs of disaffection to be noted among a small body of epidemiologists; disaffection with the neat and final assumption that the discovery of the *materies morbi* and of the methods and agents of their transmission resolved all the problems of epidemiology. The influenza pandemic inspired these dissidents with greater courage. Crookshank (F. G.), Greenwood (M.), Goodall (E. W.), and Hamer (Sir W. H.)** are the names outstanding among those who since 1918 "aroused greatly increased interest in

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* *Epidemiology Historical and Experimental* by Major Greenwood (Herter Lectures for 1931—Johns Hopkins Press, Baltimore, 1932).

** F. G. Crookshank: Chadwick Lectures, 1918. (Abst.): *Med. Press & Circ.*, 1918 clvii, 291; 310; 329—M. Greenwood: Sydenham as an epidemiologist, *Proc. Roy. Soc. Med.*, 1918-19, xii, Epidem. Sect., 55, 61—E. W. Goodall: The epidemic constitution, *Proc. Roy. Soc. Med.*, 1927-28, xxi, Epidem. Sect., I.

the study of epidemics from the natural history point of view, and tended to discourage meek acceptance by epidemiologists of a belief that all that was required of them was to rewrite epidemiology in terms of causal organisms."*

In 1925 F. G. Crookshank spoke up in fine sarcasm:

> "Whilst leaving the bacteriologists to pursue their researches to a successful issue in the seclusion of their own laboratories–for it were impious to believe that persons who ignore clinical and epidemiological data are not the predestined solvers of clinical and epidemiological problems–it may be profitable to discuss briefly two questions that, although nowadays regarded–at any rate in the best medical circles–as hardly worthy of scientific investigation, have nevertheless engaged attention since the earliest ages. These questions are, first, that of the periodicity of the recurrent pestilence we now call influenza, and, secondly, that of the dependence of these recurrences upon, or their correlation with, what used to be called telluric and cosmic influences."**

The exploration of these two problems, the periodicity of recurrent pestilences, and their dependence or correlation with "what used to be called telluric and cosmic influences" now yields astonishing and illuminating information; astonishing because unanticipated; illuminating because it conforms with our best knowledge in medicine.

In the effort to trace the periodicity of recurrent pestilence one comes upon the realization that history presents a spectacle which can be properly described as "a succession of new plagues for old." This realization invalidates old beliefs, for it has been common to think of historical time in relation to epidemics as divisible into two portions: one enormously long, and the other comparatively short. The segmental line which separates these time portions corresponds to the period of the discovery of the pathogenic microörganisms. Thus the antecedent, earlier, greater stretch of time is characterized as that period during which the epidemic diseases ravaged a helpless mankind, while the later period is labeled the age in which mankind by means of modern science, and most notably through all that goes under the name of bacteriology and immunology, mastered, one, by one, the plagues of antiquity. This characterization of time-experience is misleading and

* Sir William Hamer: *Epidemiology Old and New*, London, Kegan Paul, 1928.
** F. G. Crookshank: *Epidemiological Essays*, London, Kegan Paul, 1930.

erroneous. History, to repeat, presents rather a continuous pageant of plagues, the unbroken succession of new plagues for old.

The plagues of antiquity cannot be lumped together. True, some among them, for instance bubonic plague and influenza, are as old as mankind. But others are distinctly of later origin, and some are very modern indeed. Bearing in mind that we are considering diseases in epidemic form, and *not* diseases as nosographic entities, we cannot help but recognize some herd diseases to be what the Germans call "Zivilisationsseuche," plagues of modern civilization. Among such we can list tuberculosis, cholera, typhoid, diphtheria, scarlet fever, and cholera infantum. This is not a complete list, and to it should perhaps be added certain of the psychological disorders, notably schizophrenia. But it is long enough a list to illustrate our thesis. Among the ancient epidemic diseases, those prevalent before the Christian era, we can list bubonic plague, malaria, and typhus, while during the medieval ages we can count smallpox, leprosy, syphilis, and influenza. It is pertinent to bear in mind that all of these disease entities very probably, and most likely existed since the most ancient days. None of them is assumed to have come into being within historical time. Only as *epidemic diseases* are some certain ones labeled new, or recent. Hence it is a provocative and pertinent problem that confronts us, this problem of the succession of plagues, the demarche of new plagues for old. And, where else can we hopefully look for the solution of this problem but among "what used to be called telluric and cosmic influences." Granting that the "contagium vivum" was ever present, as appears to have been certainly the case with the tubercle bacillus, why was it, for example, that tuberculosis did not achieve the magnitude of a great epidemic disease until the Eighteenth Century?* Why was not Europe plagued by cholera, or diphtheria, or typhoid until what we call modern civilization became well advanced?

There are some, of course, who deny the validity of these questions; who maintain that Europe was indeed plagued by these diseases, but that physicians lacking diagnostic and clinical acumen did not recognize them. Such a protest is but conceit articulate, the arrogance of an ignorance that scorns the past. To this protest the gentle words of Richard Mead form a fitting retort.

"For it must be believed that the first masters of our art who

* Quotation from Brownlee.

are so careful in describing and distinguishing the signs of all diseases would not have briefly mentioned them but would have described them at length if they had but known of these at once terrible and contagious diseases."*

There can be no doubt that some epidemic diseases have been, and are, new sprung in the succession of time. And their origin is rooted in telluric and cosmic influences. Does this last statement sound like a profession of faith in astrology? Then it misleads. But who can gainsay the splendid findings of modern climatology, the painstaking work of Elsworth Huntington and of C. A. Mills, which reveal most definitely the bearing of climate upon the prevalence of disease. By telluric and cosmic influences we however intend more than climate, more than even airs, waters, and places. We intend all that was embraced by the Hippocratic *katastasis:* The entire physical environment of the people and in addition their cultural, industrial, and economic status.

I offer a brief and somewhat tentative illustration as to how changes in telluric and cosmic influences can contribute to our understanding of the historical succession of plagues. Let us review the experiences of the European peoples, notably the English, during the last three hundred years and see what bearing they may have on the new plagues which these people experienced. The period under consideration corresponds to the development of the modern industrial system. This as we know embraces the substitution of the machine for hand tools, the growth of the factory and of the modern industrial community, and the creation of a new social class, the proletariat, the class that has but one commodity to sell, its labor power. Such in brief is the common summation of the technological, economic changes experienced during the industrial revolution. But there transpired during this period certain other changes, of "telluric and cosmic" character; changes which affected large masses of people. The import of these changes, particularly in relation to epidemiology, is little appreciated. In the industrial revolution humanity experienced an unparalleled dislocation in its environmental relationships. Never before in its history was there such population density, such prolonged and close compaction of persons in factories and slums. The industrial revolution removed large masses of people from the soil, distanced them from their food sources, changed

* Quoted by Rolleston, J. D.: *The History of The Acute Exanthemata.* (The Fitzpatrick Lectures for 1935-36) London, Wm. Heinemann Ltd., 1937.

their diets, altered their foods, bound them by an exacting discipline never before experienced. The industrial revolution broke up the rural community, disrupted the homestead, dismembered the family. For millions of human beings "airs, waters, and places" were changed, for the worse. The whole social and ethical realm was altered. Old values lost their validity, old relationships, their force and strengths. In the light of all this can we doubt but that these "telluric and cosmic influences" engendered an "epidemic constitution," which favored the rise of the "*Zivilisationsseuche*"? And, what is perhaps more significant, in that it bears on our present day medical problems, can we doubt but that in order to overcome these plagues, the *epidemic constitution* must be altered? It is interesting to observe for how long this was a belief shared by the more profound students of epidemiology, albeit the others did not know or understand it. Sydenham groped about it, but never seemed to grasp it clearly, though Greenwood believes he did. In his essay on *Sydenham as an Epidemiologist* Greenwood states:

> "The bacteriologist—or, at least, his popular exponent—holds that all diseases can be attacked and conquered seriatim by specific measures; isolate the organism, "stamp it out" or procure an artificial immunity and that disease is "conquered." But if my interpretation of Sydenham's constitutions is correct, all that can be achieved in this way is either to reduce the number of stocks upon which a stationary fever may be grafted or to reduce the number of stationary fevers, leaving the stocks upon which the remainder may be grafted untouched. Naturam expellas furca, tamen usque recurret, hence Watt's theory of substitution, and Sydenham's constitutions. So the problem of preventive medicine becomes wider and we are led to ask whether what is wrong with the unhealthy may not be not infection with this or that germ but—unhealthiness, even as the chief trouble of the poor is not addiction to public houses but just plain poverty."*

William Farr also had a faint appreciation of the dominant significance of the epidemic constitution, for in his Thirtieth Annual Report he wrote:

> "It is, however, by no means proved that the general mortality under unfavourable sanitary conditions is much reduced by render-

* M. Greenwood: Sydenham as an epidemiologist, *Proc. Roy. Soc. Med.*, Sect. of Epidem., London, 1919, vol. xii, parts i & ii.

ing a child insusceptible of one type, while he remains exposed to all other types of zymotic disease."*

Dr. Ozanam writing in 1817 differentiated clearly between the epidemic proper and the epidemic constitution. He defined the epidemic constitution as "an indeterminate period during which diseases occur, which though they seem to have different characteristics; nevertheless, have the same origin and the same diathesis. It is an unique disorder of which the various forms are, so to say, only symptoms and which requires only one general method of treatment."**

Again Ozanam states:

"The epidemic constitution has a more general influence upon the human being, but its effect is felt only in an irregular and diversified manner producing a variety of diseases; whereas the effect of the real epidemic is more direct, more uniform and more marked and neither hidden nor disguised as that of the former."***

All of these authors, and others beside, sensed the significance of the epidemic constitution, and defined its nature with varying degrees of acuteness. Most of them conceived of the epidemic constitution in the narrower meaning of telluric and cosmic influences, in terms principally of climatological and terrestrial factors. They knew there was more than these elements in the epidemic constitution, but they did not know the nature of the unknown "more." They could not even conceive of them. They, as all medical men, then thought of noxious states as due to the presence and operation of inimical agents or forces. They could not conceive of morbidity arising from the *absence* of subtle and essential factors. But then this realization, this recognition of disease resulting from a minus rather than from a plus state is the most recent achievement of medical science.

It is rooted in the epoch marking discoveries in the realms of endocrinology and of nutrition. This matter commands our attention, for in it lies much of the account for the vain gropings of the epidemiolo-

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* Quoted by M. Greenwood: *Epidemics and Crowd-Diseases.* London, William & Norgate Ltd., 1935.

** "Une constitution épidémique est un espace de temps indéterminé durant lequel règnent des maladies qui, quoique d'un caractère différent en apparence, n'en ont pas moins toutes la même origine et la même diathèse. C'est une maladie unique, dont les formes variées ne sont, pour ainsi dire, que des symptômes, et qui n'exige qu'une seule méthode générale de traitement." J.A.F. Ozanam: *Histoire médicale générale et particulière des maladies épidémiques, contagieuses et épizootiques.* Paris, Lyon, 1817, p. 40.

*** "La constitution épidémique a une influence plus générale sur l'espèce humaine; mais son action ne se fait sentir que d'une manière irrégulière et diversifiée, ce qui produit la variété des maladies qui en dérivent; au lieu que l'épidémie a la sienne plus directe, plus uniforme et plus marquée sur les individus qu'elle attaque, et cette action n'est point latente ou masquée comme dans la première." J.A.F. Ozanam: *Histoire médicale générale et particulière des maladies épidémiques, contagieuses et épizootiques.* Paris, Lyon, 1817, p. 42.

gists of the preceding centuries for the unknown factors of the epidemic constitution. They searched man's realm for a something that was not there, in a manner that could not reveal it. They sought for a positive entity. They contemplated biological man as the stationary passive fixed entity upon whom the forces of the universe play their mysterious will. This viewpoint can be witnessed in two remotely diverse authors. Ludwig Edelstein in a most interesting philological analysis of the Hippocratic book ΠΕΡΙ ΑΕΡΩΝ is distressed by Hippocrates' preoccupations with the healthy man. Edelstein contends that "To be healthy means: not to be ill," the life of the healthy, he believes, does not concern the physician. The Greek physician's conviction that health has no being but is rather a perpetual development, he labels as something strange to modern people. The whole of this brilliant study, I might add, misconceives the substance and intent of the book *Airs-Waters-Places*. But Edelstein only shares in the reigning beliefs that disease is the positive state, that it is the resultant of aggressive forces which assault man's constitution, that health is only the absence of disease.

Von Behring is the other author whom we may call in witness. In the introduction to his *Gesammelte Abhandlungen zur ätiologischen Therapie von ansteckenden Krankheiten,* von Behring states his credo in the following words:

> ". . . For we are of the opinion that in combating diseases we can achieve more by attacking the causes of disease than by an attack on the living cells and organs."
>
> "Until now we only know that even the best intended, direct attacks on living cells and organs in order to animate or to stimulate them into a state of modified activity, are more likely to harm the cells and organs, than to bestow upon them more health and resistance."*

We know today that it is eminently possible to influence the living cell. We know that to a very great extent the competence of the specific disease-producing agents to injure the living body depends upon the telluric and cosmic influences which antecedently affected the living body. These influences are collectively embraced in the epidemic constitution.

By all these considerations, and by their implications, suggested but

* E. Behring: *Gesammelte Abhandlungen zue ätiologischen Therapie von ansteckenden Krankheiten.* Leipzig, Georg Thieme, 1893, p. LXX, LXXI.

not elaborated in this presentation, we are compelled to conclude that what Hippocrates intended by *katastasis* is the more important factor in epidemic diseases, that modern medical advances have validated his contentions, and have elaborated on the components of the epidemic constitution.

Finally we sum up the results of our study in this dictum. To the extent that medicine fails directly and indirectly to ameliorate the interrelationships of man and his life's realm, it can succeed only in deferring mortality but not in decreasing morbidity, and it may be taken as a corollary that to the extent that mortality is deferred, and life prolonged, to that extent is morbidity multiplied and increased.

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Nashville, Vanderbilt Univ. Press, [1942], 310 p.

Canadian Public Health Association. *Manual for sanitary inspectors.* 6. ed.
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Committee for the Study of the Care and Education of Physically Handicapped Children in the Public Schools of the City of New York. *Report of the Sub-Committee on Cardiac Classes and the Care of Cardiac Children.*
[N. Y.], Board of Education, [1941?], 99 p.

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Great Britain. War Office. Army Medical Department. *Memoranda on medical diseases.*
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Kennedy, J. W. & Campbell, A. D. *Vaginal hysterectomy.*
Phil., Davis, 1942, 495 p.

Key, J. A. & Conwell, H. E. *The management of fractures, dislocations, and sprains.* 3. ed.
St. Louis, Mosby, 1942, 1303 p.

Kitchin, D. H. *Law for the medical practitioner.*
London, Eyre, 1941, 376 p.

Kugelmass, I. N. *Superior children through modern nutrition.*
N. Y., Dutton, 1942, 332 p.

Kupper, W. H. *Medical state and national board summary.*
Paterson, N. J., Colt Press, 1942, 369 p.

Leonardo, R. A. *American surgeon abroad.*
N. Y., Froben, 1942, 235 p.

Loomis, F. M. *The bond between us; the third component.*
N. Y., Knopf, 1942, 267 p.

McCloy, C. H. *Tests and measurements in health and physical education.* 2. ed.
N. Y., Crofts, 1942, 412 p.

Maksimov, A. A. & Bloom, W. *A textbook of histology.* 4. ed.
Phil., Saunders, 1942, 695 p.

Manual of standard practice of plastic and maxillofacial surgery, prepared by . . . the National Research Council.
Phil., Saunders, 1942, 432 p.

Martindale, W. & Westcott, W. W. *The extra pharmacopoeia.* 22. ed.
London, Pharmaceutical Press, 1941, v. 1.

Moritz, A. R. *The pathology of trauma.*
Phil., Lea, 1942, 386 p.

Morris' human anatomy. 10. ed., edited by J. P. Schaeffer.
Phil., Blakiston, [1942], 1635 p.

Moschcowitz, E. *Vascular sclerosis.*
N. Y., Oxford Univ. Press, [1942], 178 p.

Motivation and visual factors; individual studies of college students by I. E. Bender, H. A. Imus, J. W. M. Rothney [and others].
Hanover, Dartmouth College Publications, 1942, 369 p.

Mottram, J. C. *The problem of tumours; the application of blastogenic agents to ciliates.*
London, Lewis, 1942, 91 p.

National Research Council. Subcommittee on Anesthesia. *Fundamentals of anesthesia.*
Chic., Amer. Med. Assoc. Press, 1942, 217 p.

Neal, J. B. [et al.] *Encephalitis; a clinical study.*
N. Y., Grune, 1942, 563 p.

New York Academy of Medicine. Committee on Public Health Relations. *Thirty years in community service,* 1911-1941.
N. Y., [N. Y. Acad. of Med., 1942], 109 p.

Nyswander, (Mrs.) D. B. *Solving school health problems.*
N. Y., Commonwealth Fund, 1942, 377 p.

Ohio Public Health Association. *Forty years of an organized fight against tuberculosis in Ohio.*
Columbus, [Ohio Pub. Health Assoc.], 1942, 116 p.

Paterson, H. J. *A surgeon looks back; the memoirs of the late Herbert John Paterson.*
London, Epsworth Press, [1941], 253 p.

Piney, A. *Sternal puncture.*
London, Heinemann, 1941, 77 p.

Preventive medicine in modern practice; edited under the auspices of the Committee on Public Health Relations of The New York Academy of Medicine. [3. ed.]
N. Y., Hoeber, [1942], 851 p.

Regli, A. C. *The Mayos.*
N. Y., Messner, [1942], 248 p.

Rice, T. B. *A Textbook of bacteriology.* 3. ed.
Phil., Saunders, 1942, 560 p.

Rorschach, H. *Psychodiagnostics.*

Berne, Heuser, [1942], 226 p.

Rosenberg, H. R. *Chemistry and physiology of the vitamins.*
N. Y., Interscience Publishers, 1942, 674 p.

Scharlieb, (Dame) M. A. D. (Bird). *Change of life.* [New and rev. ed.]
London, Faber, [1941], 94 p.

Scott, G. D. *Heredity, food and environment in the nutrition of infants and children.*
Boston, Chapman, [1942], 778 p.

Sheldon, W. H. *The varieties of temperament.*
N. Y., Harper, 1942, 520 p.

Sorsby, A. *Medicine and mankind.*
London, Faber, [1941], 263 p.

Taylor, C. M. *Food values in shares and weights.*
N. Y., Macmillan, 1942, 92 p.

Thorek, M. *Plastic surgery of the breast and abdominal wall.*
Springfield, Ill., Thomas, [1942], 446 p.

Wangensteen, O. H. *Intestinal obstructions.* 2. ed.
Springfield, Ill., Thomas, [1942], 484 p.

Warkentin, J. & Lange, J. *Physician's handbook.* 2. ed.
Chic., Univ. Med. Publishers, [1942], 281 p.

Webster, L. T. *Rabies.*
N. Y., Macmillan, 1942, 168 p.

Willard, J. H. *Digestive diseases in general practice.*
Phil., Davis, 1942, 449 p.

Zechmeister, L. & Cholnoky, L. *Principles and practice of chromatography.*
London, Chapman, 1941, 362 p.

DEATH OF FELLOW

Ill, Edward Joseph: 1004 Broad Street, Newark, New Jersey; born in Newark, May 23, 1854; died in Island Heights, New Jersey, June 9, 1942; graduated in medicine from the College of Physicians and Surgeons, Columbia University in 1875; elected a Fellow of the Academy February 1, 1894.

Dr. Ill was formerly surgeon to Woman's Hospital and medical director of St. Michael's Hospital; gynecologist, supervising obstetrician and trustee of St. Barnabas Hospital; consulting gynecologist, Beth Israel Hospital, Newark, All Soul's Hospital, Morristown, Mountainside Hospital, Montclair, and the Rahway Memorial Hospital, Rahway. He was a Fellow and member of the Board of Governors of the American College of Surgeons, a Fellow of the American Medical Association, past president of the Essex County Medical Society and the Medical Society of the State of New Jersey; a diplomate of the American Board of Obstetrics and Gynecology; in 1893 vice-president, in 1899 president, and member of the executive council from 1901 to 1903 of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; vice-president for New Jersey of the Pan American Medical Congress in 1893; member of the Southern Surgical Association, chairman for the State of New Jersey of the American Society for the Control of Cancer; a member of the Board of Education of Newark from 1878 to 1880; for many years state director of the Prudential Life Insurance Company of America; and a member of the American Radium Society, the American Association for Cancer Research, the Southern Surgical Society, the New Jersey Surgical Society and the Academy of Medicine of Northern New Jersey.